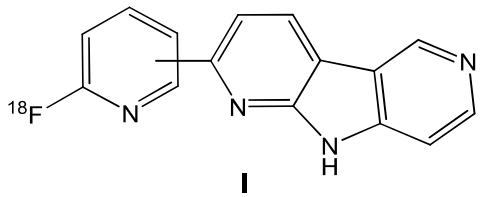
Figure 4: Setup of the IBA Synthera synthesizer

Summary

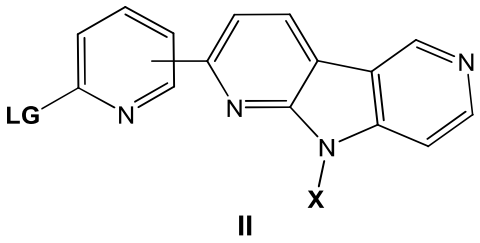
In one aspect, the present disclosure relates to a method of preparing a compound of the formula **I**



I

comprising the steps of

A) reacting a compound of the formula **II** with a ^{18}F fluorinating agent



II

,

wherein **X** is H or **PG**,

LG is a leaving group, and

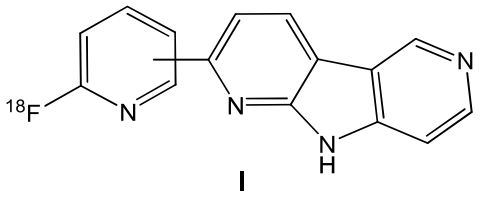
PG is an amine protecting group selected from carbobenzyloxy, (p-methoxybenzyl)oxycarbonyl, tert-butyloxycarbonyl, 9-fluorenylmethyloxycarbonyl, benzyl, p-methoxybenzyl, 3,4-dimethoxybenzyl, p-methoxyphenyl, triphenylmethyl, methoxyphenyl diphenylmethyl and dimethoxytrityl, and

B) optionally, if **X** is **PG**, cleaving the protecting group **PG**, and

C) subjecting the resultant compound of the formula **I** to high-performance liquid chromatography (HPLC) using a mobile phase comprising a mixture of ethanol and water.

The present disclosure relates to the following items:

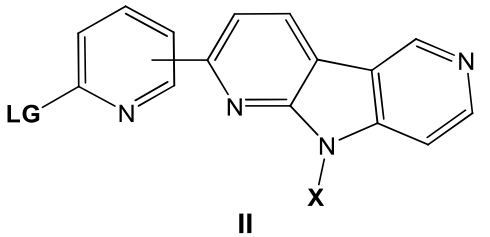
1. A method of preparing a compound of the formula **I**



I

comprising the steps of

A) reacting a compound of the formula **II** with a ^{18}F fluorinating agent



II ,

wherein **X** is H or **PG**,

LG is a leaving group, and

PG is an amine protecting group, and

B) optionally, if **X** is **PG**, cleaving the protecting group **PG**, and

C) subjecting the resultant compound of the formula **I** to high-performance liquid chromatography (HPLC) using a mobile phase comprising ethanol and water.

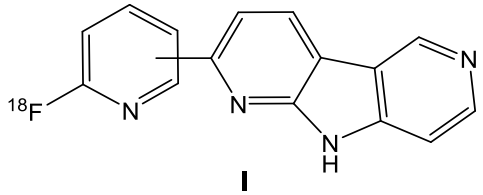
2. The method according to item 1, wherein **X** is **PG**, step B is absent and the protecting group **PG** is cleaved in step A.

3. The method according to item 1, wherein **X** is **PG** and the protecting group **PG** is cleaved in step B.

4. The method according to any one of items 1 to 3, wherein the ratio of ethanol to water in the mobile phase is from about 5/95 v/v to about 80/20 v/v.

CLAIMS

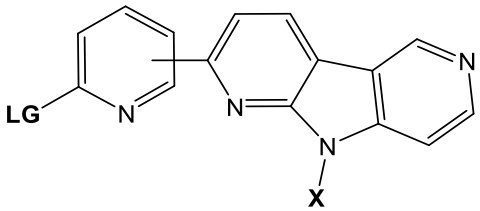
1. A method of preparing a compound of the formula **I**



I

comprising the steps of

A) reacting a compound of the formula **II** with a ^{18}F fluorinating agent



II

,

wherein **X** is H or **PG**,

LG is a leaving group, and

PG is an amine protecting group selected from carbobenzyloxy, (p-methoxybenzyl)oxycarbonyl, tert-butyloxycarbonyl, 9-fluorenylmethyloxycarbonyl, benzyl, p-methoxybenzyl, 3,4-dimethoxybenzyl, p-methoxyphenyl, triphenylmethyl, methoxyphenyl diphenylmethyl and dimethoxytrityl, and

B) optionally, if **X** is **PG**, cleaving the protecting group **PG**, and

C) subjecting the resultant compound of the formula **I** to high-performance liquid chromatography (HPLC) using a mobile phase comprising a mixture of ethanol and water.

2. The method according to claim 1, wherein X is PG, step B is absent and the protecting group PG is cleaved in step A or wherein X is PG and the protecting group PG is cleaved in step B.

3. The method according to claim 1 or 2, wherein the ratio of ethanol to water in the mobile phase is from 5/95 v/v to 80/20 v/v.

4. The method according to any of claims 1 to 3, wherein the pH of the mobile phase is from 0 to 8, preferably 1 to 3.

5. The method according to any of claims 1 to 4, wherein the mobile phase further comprises a buffer, which is preferably selected from alkali metal dihydrogen phosphates, di alkali metal hydrogen phosphates, tri alkali metal phosphates, alkali metal acetates, alkali metal formates, and mono/di/tri alkali metal citrates.

6. The method according to any one of claims 1 to 5, wherein the high-performance liquid chromatography (HPLC) is conducted under a pressure of $5*10^6$ to $4*10^7$ Pa (50 to 400 bars), preferably $5*10^6$ to $25*10^6$ Pa (50 to 250 bar).

7. The method according to any one of claims 1 to 6, wherein the high-performance liquid chromatography (HPLC) results in a fraction comprising the compound of the formula I and this fraction is subjected to a step D) sterile filtration.

8. The method according to any one of claims 1 to 7, wherein the method does not comprise solid phase extraction of the compound of the formula I after step C, preferably wherein the method does not comprise solid phase extraction of the compound of the formula I before or after step C.

9. The method according to any one of claims 1 to 8, wherein the compound of the formula I is not subjected to chromatography after the high-performance liquid chromatography (HPLC) of step C, preferably wherein the compound of the formula I is not subjected to chromatography other than the high-performance liquid chromatography (HPLC) of step C.