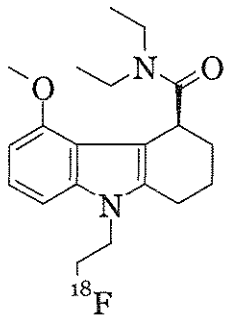
PBR.

Summary ~~of the Invention~~

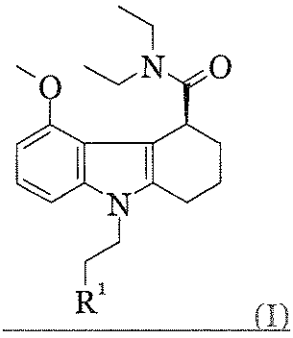
The present ~~invention~~disclosure provides a PET tracer that retains the advantageous properties of the known tricyclic indole PET tracer, and also has a number of improved properties. It has been demonstrated that, in comparison to a known tricyclic PET tracer, the PET tracer of the ~~invention~~disclosure has improved binding affinity for PBR, marginally improved metabolism profile with a high proportion of activity at 60 minutes post-injection representing activity in the brain, and significantly improved specific binding to PBR-expressing tissues. The present ~~invention~~disclosure also provides a precursor compound useful in the preparation of the PET tracer of the ~~invention~~disclosure, as well as methods for the preparation of said precursor compound and said PET tracer. Also provided by the present ~~invention~~disclosure is a radiopharmaceutical composition comprising the PET tracer of the ~~invention~~disclosure. Methods for using the PET tracer and the radiopharmaceutical composition are also provided.

In one aspect, there is provided a positron-emission tomography (PET) tracer having the following chemical structure:



.

In another aspect, there is provided a precursor compound for the preparation of the PET tracer as defined above wherein said precursor compound is of Formula I:

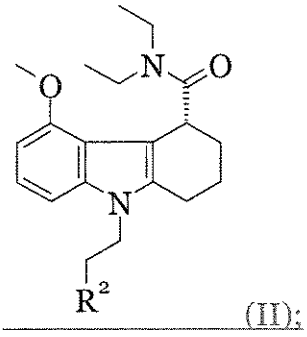


(I)

wherein R^1 is hydroxyl or is a leaving group.

In another aspect, there is provided a first method to prepare the precursor compound of Formula I as defined above wherein said method comprises:

(i) providing a racemic mixture of said precursor compound of Formula I and a compound of Formula II:



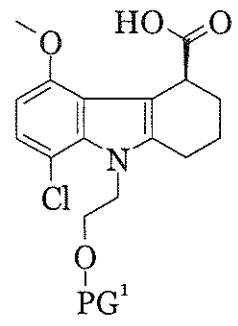
(II);

wherein R^2 is as defined for R^1 above, and R^1 and R^2 are the same;

(ii) separating said precursor compound of Formula I from said compound of Formula II.

In another aspect, there is provided a second method to prepare the precursor compound of Formula I as defined above wherein said method comprises:

(i) providing a compound of Formula III:

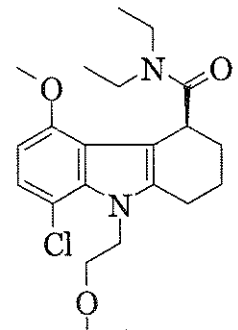


(III)

wherein PG^1 is a hydroxyl protecting group;

(ii) converting said compound of Formula III to its corresponding acid chloride;

(iii) reacting the acid chloride obtained in step (ii) with diethylamide to obtain a compound of Formula IV:



(IV)

wherein PG^2 is a hydroxyl protecting group and is the same as PG^1;

(iv) deprotecting the compound of Formula IV obtained in step (iii) to obtain the hydroxyl derivative;

(v) optionally adding a leaving group as defined above for Formula I;

wherein a precursor compound of Formula I results from either step (iv) or step (v).

In another aspect, there is provided a method to prepare the PET tracer as defined above wherein said method comprises reaction of the precursor compound of Formula I as defined above with a suitable source of ^{18}F.

In another aspect, there is provided a cassette for carrying out the method as defined above comprising:

i) a vessel containing the precursor compound as defined above; and,

ii) means for eluting the vessel of step (i) with a suitable source of ^{18}F as defined above.

In another aspect, there is provided a radiopharmaceutical composition comprising the PET tracer as defined above together with a biocompatible carrier suitable for mammalian administration.

In another aspect, there is provided a PET imaging method to determine the distribution and/or the extent of PBR expression in a subject, wherein said method comprises:

i) administering to said subject the PET tracer as defined above;

ii) allowing said PET tracer to bind to PBR in said subject;

iii) detecting signals emitted by the ^{18}F comprised in said bound PET tracer;

iv) generating an image representative of the location and/or amount of said signals; and,

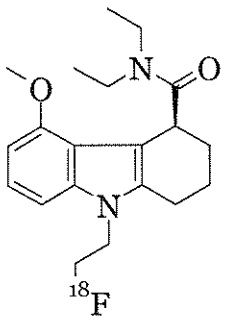
v) determining the distribution and extent of PBR expression in said subject wherein said expression is directly correlated with said signals.

In another aspect, there is provided a method for diagnosis of a condition in which PBR is upregulated wherein said method comprises the PET imaging method as defined above, together with a further step (vi) of attributing the distribution and extent of PBR expression to a particular clinical picture.

Detailed Description of the Invention

PET Tracer

In one aspect, the present invention provides a positron-emission tomography (PET) tracer having the following chemical structure:



wherein the chiral centre has (S) configuration.

A "PET tracer" is a chemical compound that comprises a positron-emitting