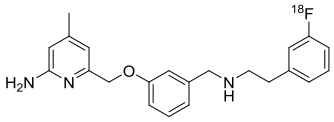
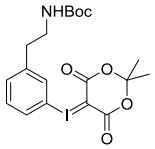
## Abstract

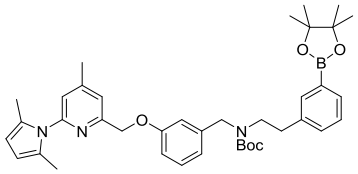
Nitric oxide (NO), an important signalling molecule, is synthesized from L-arginine by three isoforms of NO-synthase (NOS). Its overproduction has been associated with neurodegenerative disorders. Therefore, developing selective inhibitors of iNOS or nNOS is of great interest for decoding neurodestructive key factors. Suitable $^{18}$F-labelled analogues would allow for investigation of the NOS-function by molecular *in vivo* imaging with positron-emission-tomography. Potentially, the highly selective nNOS inhibitor 6-((3-((3-fluorophenyl-ethylamino)methyl)phenoxy)-methyl)-4-methyl-pyridine-2-amine (**1**) is a suitable compound for labelling with no-carrier-added (n.c.a.) [$^{18}$F]fluoride, complementing the established iNOS inhibitor 6-(2-[$^{18}$F]fluoropropyl)-4-methylpyridine-2-amine.




**[$^{18}$F]1**




**2**




**3**

Presently the radioorganic syntheses of n.c.a. $^{18}$F-labelled products are practically limited to nucleophilic procedures. Based on cyclic voltammetric measurements an electrochemical synthesis of n.c.a. *N*-[$^{18}$F]fluorobis(trifluoromethylsulfonyl)imide ($Tf_2N$-[$^{18}$F]F) was attempted. The following conversion of the electrosynthetic product with an activated arene led to an $^{18}$F-labelled derivative. In this early developmental stage, a production of an n.c.a. electrophilic $^{18}$F-fluorinating reagent from [$^{18}$F]fluoride appears probable. For the effective labelling of NOS-inhibitors, however more sophisticated labelling methods had to be chosen.

With regard to the nNOS-Inhibitor **[$^{18}$F]1** a built-up radiosynthesis based on a iodonium ylide **2** as precursor was attempted. The activated aromatic system was efficiently and regionselectively labelled with n.c.a. [$^{18}$F]fluoride in 79 % radiochemical yield (RCY). After conversion by reductive amination and microwave assisted displacement of the protecting groups the desired nNOS inhibitor was obtained in 15 % RCY. Alternatively, for a simplified late-stage $^{18}$F-labelling procedure the corresponding boronic ester precursor **3** was synthesized and labelled starting by novel copper(II) mediated n.c.a. $^{18}$F-fluorination and led to the same RCY.

After optimizing the radiolabelling procedure of the established iNOS inhibitor 6-(2-[$^{18}$F]Fluorpropyl)-4-methylpyridin-2-amin, now there are two highly selective NOS-inhibitors available for preclinical *in vivo* evaluation studies.