CLICK CHEMISTRY FOR ^{18}F LABELLING OF BIOACTIVE COMPOUNDS

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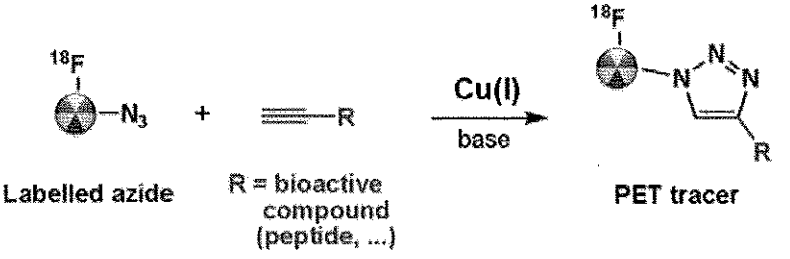
Positron Emission Tomography (PET) is gaining increased importance in the field of drug development as a powerful *in vivo* pharmacological imaging modality. This high sensitivity technique is particularly well suited to carry out quantitative biodistribution (eg. microdosing) and drug occupancy studies[1, 2].

Fluorine-18 is by far the most used positron emitting radionuclide in PET thanks to his appropriate physical and nuclear properties ($t_{1/2}$ = 110 min ; E_{beta+} = 0.635 MeV). Numerous ^{18}F labelling strategies of bioactive molecules have been developed but generally require several protection / deprotection steps which are not always compatible with the stability of the substrate and often imply extended total radiosynthesis time.

In this context, the Cu(I) catalyzed 1,3 dipolar Huisgen cycloaddition between an alkyne and an azide (a typical "click" reaction[3], scheme 1) appears as a new promising alternative, especially in the case of peptide/protein radiolabelling [4,5]. Main advantages of this strategy are high yields, mild reaction conditions, water compatibility and *in vivo* stability of the 1,2,3-triazole formed. Moreover, in the case of peptides, the very high specificity of this alkyne - azide reaction permits to avoid the need of protecting others functional groups present on the peptidic backbone beforehand.



Scheme 1

This strategy begins with the insertion of the alkyne and azide functions onto the structure of each partner of the "click" reacting pair. In this regard, we developed an original and automated four steps radiosynthesis of a ^{18}F labelled azide, namely [^{18}F] 1-(azidomethyl)-4-fluorobenzene, with a 50 % radiochemical yield (decay corrected). Preliminary results on the conjugation of this compound to alkyne bearing model compounds by click chemistry will be reported as well.

References

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