Molecular imaging techniques allow us to see biological processes as they happen inside the human body. Positron electron tomography (PET) is one such technique. It is currently used for the diagnosis of cancers, and is being increasingly used for the diagnosis of heart conditions. PET can also be used for the diagnosis of neurological disorders such as Alzheimer’s Disease, Parkinson’s Disease and depression. Labels containing positron-emitting radioisotopes are injected into the body before PET imaging. Fluoride-18 is one of the leading positron-emitting radiotracers used for the labeling of biomolecules, since it has a half-life close to 2 hours and offers the highest potential resolution in a PET camera.

The synthesis of 18F-labeled radiotracers can be difficult. Traditional electrophilic fluorination methods are costly and result in low radiochemical yields. 18F-labeling of PET radiotracers can be achieved by synthesizing 18F-fluoroarene tracer precursors, which may then be applied to label the relevant biomolecules. Fluoroarene precursors can be obtained from the nucleophilic aromatic substitution of diaryliodonium salts, which have excellent leaving-group ability, but elaborate syntheses with harsh conditions are still required and often result in poor fluorination selectivity. There is a need to develop mild reaction conditions to make the synthesis of PET radiotracer precursors from diaryliodonium salts easier and more cost-effective, while increasing the regioselectivity of radiofluorination. The development of new PET radiotracers is likely to increase the utilization of PET imaging for disease diagnosis, especially brain-related disorders. Although there are several FDA-approved radiotracers for beta amyloid plaque detection, no radiotracers are currently approved for the monitoring of dopamine activity, which could be used to properly diagnose Parkinson’s Disease and depression. The PET diagnostics market revenue is expected to grow from $236.7 million in 2012 to $705.4 million in 2019, at a CAGR of 16.9%.

Transition metal-catalyzed 18F-fluorination of diaryliodonium salts

A practical, rapid and highly regioselective Cu-catalyzed synthesis method has been developed for the radiofluorination of diaryliodonium salts with good radiochemical yields. Synthesis of fluoride-18-labeled electron rich, neutral and deficient fluoroarenes is achieved under mild conditions, enabling access to 18F-labeled radiopharmaceuticals that would be difficult if not impossible to access using traditional radiofluorination methods. Two such chemicals, Fluorodopa and F-PHE, which can be used to monitor dopamine activity in patients with Parkinson’s disease, were synthesized following this protocol. This technology is readily translatable to non-specialist radiochemistry laboratories around the world, since the catalysts used to make the fluoroarenes are commercially available and do not require the use of a drybox during synthesis.

Applications

- Synthesis of fluorine-18 labeled radiopharmaceuticals for PET
- Drug development and monitoring
Advantages

- Mild synthesis reaction conditions tolerate electron rich, neutral and deficient substrates.
- Synthesis method is compatible with wide range of functional groups.
- Cost-effective, rapid, highly selective radiofluorination

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