M. HUIBAN, M. TREDWELL, S. MIZUTA, Z. WAN, X. ZHANG, T. L. COLLIER, V. GOUVERNEUR,* J. PASSCHIER* (IMPERIAL COLLEGE LONDON AND UNIVERSITY OF OXFORD, UK; GLAXOSMITHKLINE, SHANGHAI, P. R. OF CHINA; ADVION BIOSYSTEMS, ITHACA, USA)

A Broadly Applicable \( ^{18}\text{F} \)Trifluoromethylation of Aryl Iodides and Heteroaryl Iodides for PET Imaging


\[ ^{18}\text{F} \]Trifluoromethylation of Aryl and Heteroaryl Iodides

**Significance:** The authors disclose the easy and broadly applicable late-stage \( ^{18}\text{F} \)trifluoromethylation of various aryl and heteroaryl iodides using methyl chlorodifluoroacetate, CuI, TMEDA, and \( ^{18}\text{F} \)fluoride. The \( ^{18}\text{F} \)trifluoromethylated (hetero)aryl, which serve as \( ^{18}\text{F} \)-PET (positron emission tomography) tracers, are obtained in good yields.

**Comment:** Usually, access to \( ^{18}\text{F} \)-labelled probes is limited by the short half-life of \( ^{18}\text{F} \) and the small availability of parent \( ^{18}\text{F} \) sources that show a suitable reactivity, such as \( ^{18}\text{F} \)F\(^{-}\) and \( ^{18}\text{F} \)F\(_{2}\). Furthermore, this operational simple \( ^{18}\text{F} \)CuCF\(_{3}\)-based strategy excludes the tedious preparation of complex organometallic precursors and may be performed on air. The active \( ^{18}\text{F} \)CF\(_{3}\)Cu is generated in situ.

**Key words**
copper
\( ^{18}\text{F} \)trifluoromethylation
aryl iodides
heteroaryl iodides

**Category**
Metal-Mediated Synthesis

**Key words**
copper
\( ^{18}\text{F} \)trifluoromethylation
aryl iodides
heteroaryl iodides

**Selected examples:**

- \( \text{NO}_2 \): 87% yield
- \( \text{BocHN} \): 45% yield
- \( \text{CO}_2\text{Et} \): 55% yield
- \( \text{CH}_2\text{O} \): 19% yield (obtained by C–H functionalization)
- \( \text{N}\text{HCO}-\text{Bu} \): 45% yield
- \( \text{Cl} \): 38% yield
- \( \text{SN} \): 40% yield

\( \text{R} = \text{NO}_2, \text{CO}_2\text{Et}, \text{CHO}, \text{Ac}, \text{CO}_2\text{H}, \text{CN}, \text{Br}, \text{Ph}, \text{OAc}, \text{OPiv}, \text{OH}, \text{OBn}, \text{OAc}, \text{CONH}_2, \text{NH}_2, \text{NHC(O)Me}, \text{NH}_{2}\text{Boc}, \text{chiral dipeptide, chiral carbohydrate} \)

\( \text{HetAr} = \text{pyridyl, pyrazyl, quinolyl, benzothiazolyl, thienyl, uracilyl and indolyl derivatives} \)