One of the key objectives in the Gouverneur’s group is to capitalize on our expertise in synthetic fluorine chemistry by undertaking a research program aimed at changing dramatically the landscape of 18F-radiochemistry by providing radiochemists a filled toolbox of new radiosynthetic methods for the preparation of valuable radiotracers. In this project, at first trial, this proposal was to prepare electrophilic 18F-labelled *N-F* reagents of high specific activity (SA) [SA is expressed as the ratio of radioactivity relative to the mass or molar amount of the compound- critical for PET] and access their value for electrophilic 18F-fluorination. The methods for a reaction of nitrenes with nucleophilic fluorinating reagents we examined were not successful to access N-F bond formation (See, midterm report). On the course of this project, we found that branched allylic CF3 products are accessible by copper-catalyzed trifluoromethylation of allylsilanes with hypervalent iodine reagent (*Chem. Eur. J.* **2012**). In addition, the stereoselective trifluoromethylation of allysilane under photoredox catalysis also has been achieved (*Org Lett,* **2013**). This approach could extend to the application of hydrotirfluoromethylation of unactivated olefins accessing terminal trifluoromethyl compounds (*JACS* **2013**).



Furthermore, we demonstrated new radiosynthetic methods for [18F]labeling of CF3 arenes. Given the utility of 18F isotope, [18F]labeling of functionalized trifluoromethyl arenes and heteroarenes including pharmaceutical agents is extremely sought after in clinical practice. But, despite pressing and important issues, practicable methodologies for synthesis of [18F]labeling trifluoromethyl-substituted (hetero)arenes *via* a late-stage [18F]trifluoromethylation have been underdeveloped. In the year 2013, we developed two different methods accessing the (hetero)aryl**—**CF218F; Ag(I)-mediated [18F]fluorodecarboxylation of arylCF2COOH (Org Lett 2013) and alternatively cross-coupling trifluoromethylation of (hetero)aryl iodide precursors with [18F]CF3Cu complex formed from [18F]fluoride and a reagent acting as a difluorocarbene source. We herein discuss two categories: recent advances in performing trifluoromethylation of terminal olefin as a “cold” reaction and “hot” experiments accessing synthesis of [18F]labeling trifluoromethyl-substituted (hetero)arenes.

All these improvements can be used for radiosynthesis of [18F]trifluoromethylation of pharmaceutical candidates to facilitate drug development, especially for CNS diseases. Unprecedented 18F-PET tracers for clinical studies would be synthesized by using this methodology. Its operational simplicity allows for immediate use by most establishments providing they have access to basic PET chemistry infrastructure.