

Investigations into Transition Metal Catalyzed/Mediated Arene Trifluoromethylation and Fluorination Reactions

by

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献给
我最亲爱的人
我的爷爷，姥爷，姥姥
和
我的爸爸，妈妈

To my grandparents and parents

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Abstract

Aryl-CF₃ and aryl-F motifs are widely prevalent in pharmaceuticals and agrochemicals. As a result, the development of practical methods for the formation of these bonds has become an active field of research. Over the past five years, transition metal catalyzed cross-coupling between aryl-X (X = halide, organometallic, or H) and various CF₃ or F reagents has emerged as a particularly exciting approach for generating aryl-CF₃ and aryl-F bonds. Despite significant advances in this area, current methods generally suffer from limitations such as poor generality, the requirement for harsh reaction conditions, stoichiometric amounts of transition metals, and the use of costly CF₃ or F precursors. This thesis describes a variety of approaches to address some of these challenges.

Chapters 2 to 4 focus on aromatic trifluoromethylation. In particular, **Chapter 2** describes the development of two Cu-based trifluoromethylations of aryl boronic acids. A key feature of these transformations is the identification of a novel mechanistic manifold that merges transition metal-mediated activation of an organometallic reagent with trifluoromethyl radicals. Both transformations show broad substrate scope and proceed under mild reaction conditions using inexpensive CF₃ precursors.

Chapter 3 describes an exploration of AgCF₃ for C-H trifluoromethylation. The reactions of simple arenes with *in situ* generated AgCF₃ afford C-H trifluoromethylated products under mild conditions. Preliminary mechanistic studies suggest that trifluoromethyl radicals are involved in this transformation.

Chapter 4 describes investigations of facile aryl-CF₃ coupling from two unusual high oxidation state Pd(aryl)(CF₃) complexes. Detailed mechanistic studies of this

transformation were performed and could provide valuable insights for the rational design of new Pd^{II/IV}-catalyzed C–H trifluoromethylation reactions.

Chapter 5 details the development of the Cu-mediated fluorination of aryl trifluoroborates under unprecedented mild conditions. The reaction is proposed to proceed through a Cu^{I/III} pathway with a Cu^{III}(aryl)(F) complex acting as a key intermediate. An *N*-fluoropyridinium reagent was used as both oxidant and F source in this transformation.