AROMATIC C-H THIANTHRENATION: MECHANISMS AND APPLICATIONS

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INTRODUCTION

Aromatic C-H functionalization has emerged as a powerful tool, enabling the rapid derivatization of complex molecules in the late stage of synthetic process.[1] Because of its high efficiency and accuracy in synthesis, high site selectivity has long served as a desirable feature of this field. Traditionally, the realization of high site selectivity necessitated proper directing groups or substitution patterns, such as borylation and bromination.[2] Lack of these features would result in eroded selectivity. Inspired by the reactivity-selectivity principle, Ritter and coworkers successfully developed a highly selective aromatic C-H thianthrenation reaction to furnish aryl thianthrenium salts (**Figure 1**), circumventing the necessity for directing groups or predetermined substitution patterns[3]. Besides, owing to the unique oxidative and cationic properties, the aryl thianthrenium cation, as a reagent, opens up a trio of distinct applications, each rooted in divergent mechanisms.

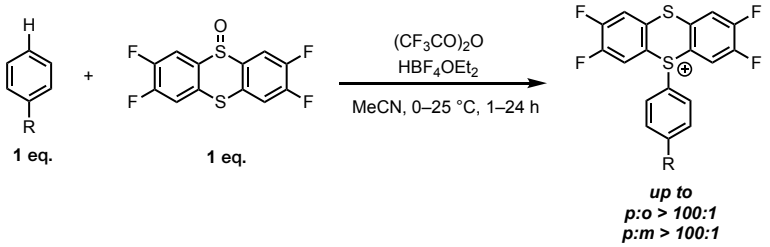
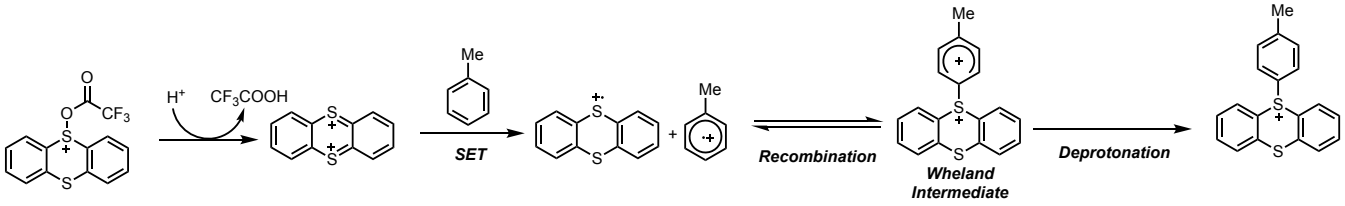


Figure 1. Highly selective aromatic C-H thianthrenation reaction.

MECHANISTIC STUDY AND THE ORIGIN OF SITE SELECTIVITY



Scheme 1. Proposed mechanism of aromatic C-H thianthrenation.

Initially, the thianthrenium radical cation ($TT^{+\cdot}$) was presumed to be the key reactive intermediate.[3] However, the observed reaction rate between $TT^{+\cdot}$ and *tert*-butylbenzene was significantly lower than expected under standard conditions, ruling out the $TT^{+\cdot}$ pathway.[4] To further investigate the role of another two potential intermediates, acylated thianthrene sulfoxide (TT-TFA^+) and thianthrenium dication (TT^{2+}), NMR study and DFT calculation was carried out (**Scheme 1**). The findings suggest that thianthrene sulfoxide (TTO) undergoes acylation by anhydride to yield TT-TFA^+. Acidic conditions prompt the release of TFA from TT-TFA^+, yielding the oxidative TT^{2+}, which then participates in a single electron

transfer (SET) with the arene, forming a radical pair. This radical pair recombines reversibly to produce the Wheland intermediate, consistent with the significant primary kinetic isotope effect (KIE) observed. The selectivity-determining step is identified as a highly exergonic deprotonation, occurring via an early transition state, resembling the Wheland intermediate in both structure and energy. The preferential formation of the *para*-Wheland intermediate, favored both electronically and sterically, accounts for the observed exquisite site selectivity.

SYNTHETIC APPLICATION OF ARYL THIANTHRENIUM SALTS

The aryl thianthrenium salts stands out as an exceptionally versatile reagents, which have three distinct functions under different reaction conditions. Primarily, they serve as cross-coupling partners in diverse transition metal-catalyzed reactions,[5] including Suzuki, Sonogashira, and Heck couplings. Their notable non-coordination with cationic Pd(II) leaves a coordination site open, a feature that enables isotopic exchange reactions under homogeneous Pd catalysis—reactions typically restricted in aryl halides.[6] Furthermore, they serve as radical precursors, facilitating transformations including trifluoromethylation, hydroxylation, and halogenation.[7] Most recently, aryl thianthrenium salts have also been identified as precursors for benzyne, expanding their utility in synthetic chemistry (**Figure 2**).[8]

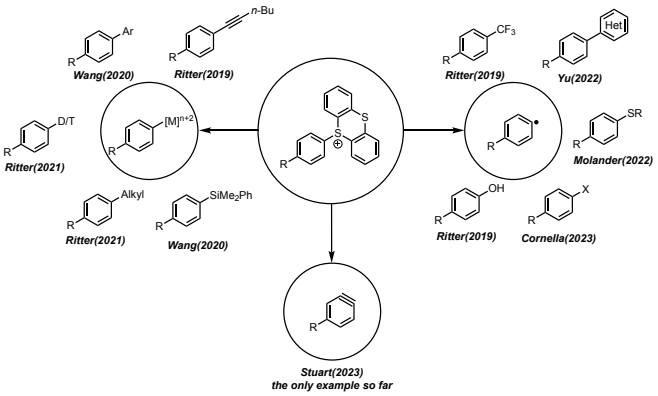


Figure 2. An overview of synthetic application

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