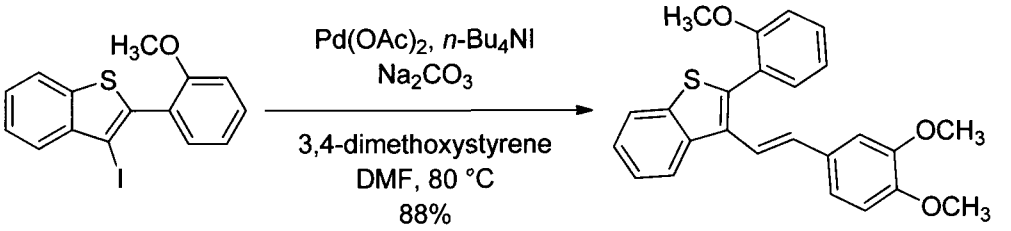
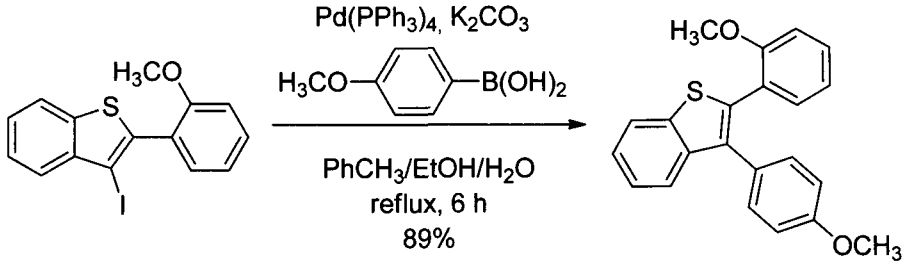
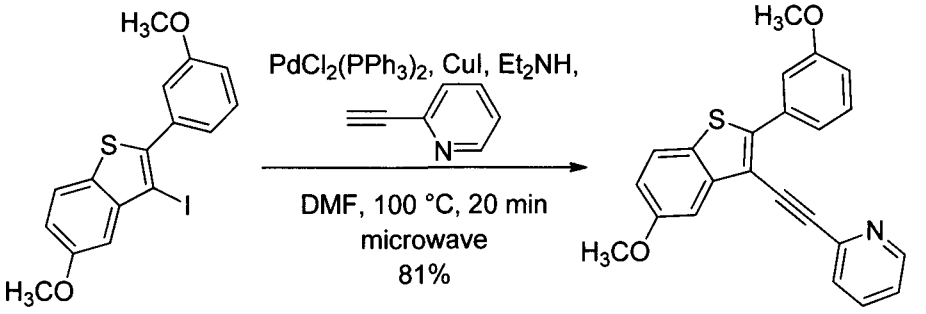
4.3.1.3 Transition Metal-Catalyzed Cross-Coupling Reactions

Cross-coupling reactions have proven to be a powerful tool in organic synthesis; this is no different for the manipulations of thiophenes and benzothiophenes.[90] The following examples, reported by Larock and co-workers, highlight the versatility of halo-benzothiophenes (synthesized via electrophilic cyclization) as substrates for various cross-coupling reactions such as the Heck, Sonogashira, and Suzuki–Miyaura reactions.[91] These compounds were synthesized to create a screening library of benzothiophene-based analogues as biologically active compounds.







Direct functionalization of the *C2* position of thiophene can be accomplished through an oxidative-Heck reaction employing palladium(II) acetate in the presence of silver carbonate. The resulting products are obtained in good to high yields with the *trans*-alkene isomer being favored. Typically less than 10% branched coupling products were observed (not shown).[92]