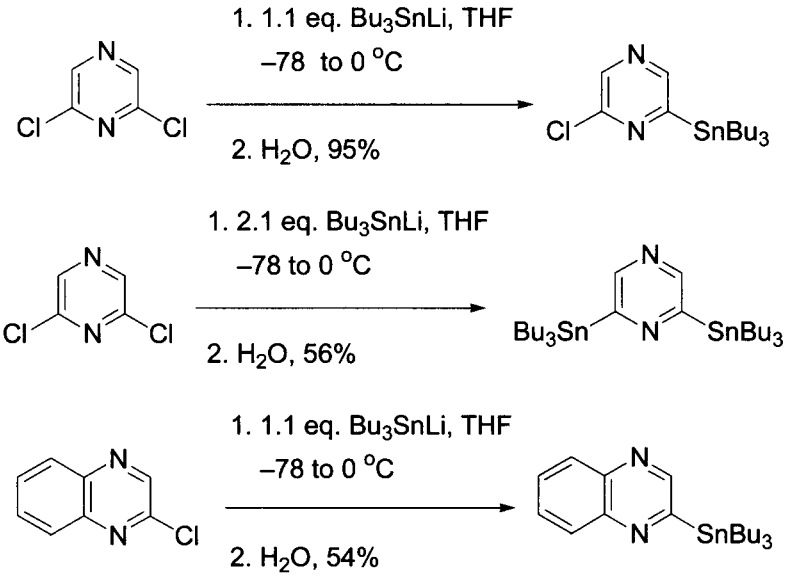

In an effort to synthesize a series of trisubstituted pyrazines to study their kinase inhibition activity, a series of regioselective substitution reaction was accomplished under two separate pathways. The first was more amenable to rapid structure activity relationships at the N_1 position. At this position a wide variety of benzylic, alkyl and amide functionalities were present.[58]

The first pathway began with a Suzuki coupling of the aryl boronate with 5-bromopyrazin-2-amine to provide the difunctional pyrazine. Halogenation α to the amino group followed by the TIPS deprotection provides a late stage intermediate that could be used for rapid screening for kinase inhibitors. Heating the diazinyl bromide in the presence of the desired amine displaces the bromide under microwave irradiation. This also causes an intramolecular nucleophilc attack by the incorporated nitrogen to one of the Boc carbonyls to provide the cyclized urea in 16–54% yield.