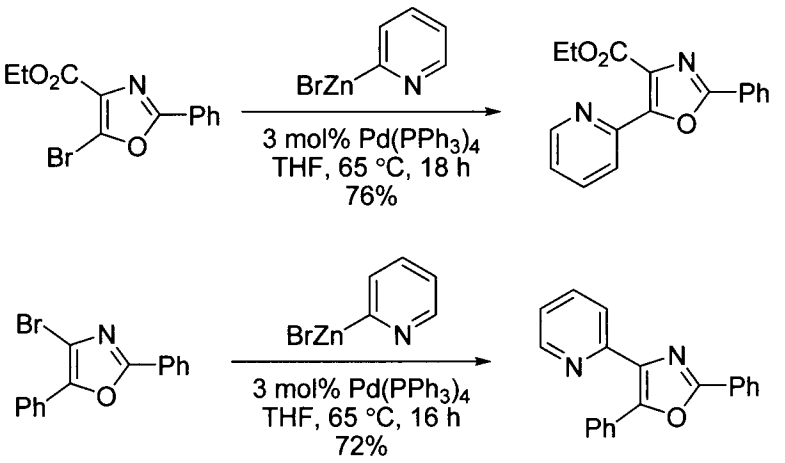
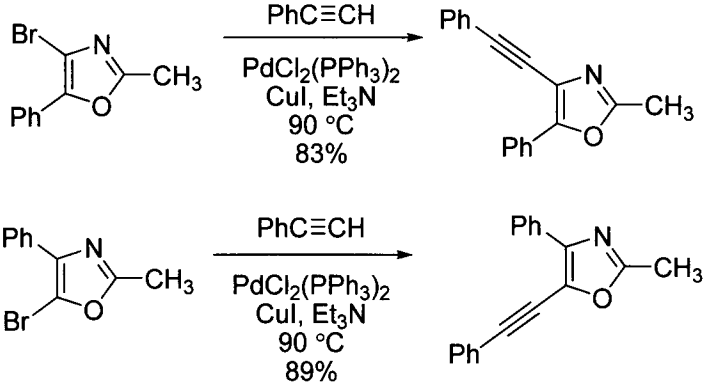


6.4.5 *Sonogashira Coupling*

Scope of the reaction

The first report of a Sonogashira coupling reaction of an oxazole was by Yamanaka in 1987.[88] Oxazoles substituted with bromine at the 4- or 5-positions were coupled with phenylacetylene yielded the alkyne in 83% and 89% yield, respectively. The Sonogashira reaction with 2-halooxazoles was not attempted; however, 2-halothiazoles and 2-halo-*N*-methylimidazoles were subjected to Sonogashira conditions. Yields in both cases were low and not synthetically useful.



Panek and co-workers showed that trifloyloxazoles react quite cleanly in Sonogashira coupling reactions.[89] The reactions require heating to 65 °C and work best with copper(I) iodide (CuI > CuBr > $(MeCN)_4CuPF_4 \approx$ CuCl). DMF or 1,4-dioxane proved to be the optimal solvents for the reaction. Under optimal conditions (CuI, Et_3N, $Pd(PPh_3)_4$, DMF), 4- and 5-