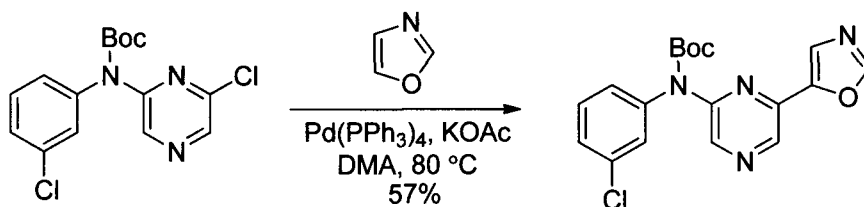
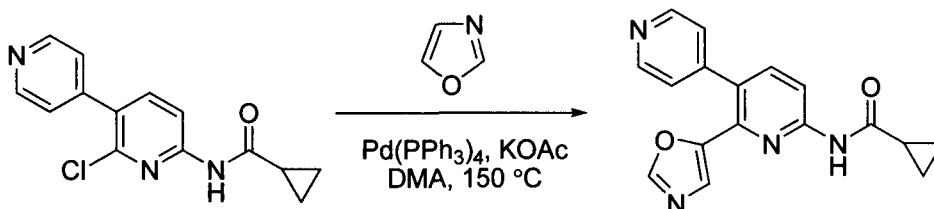


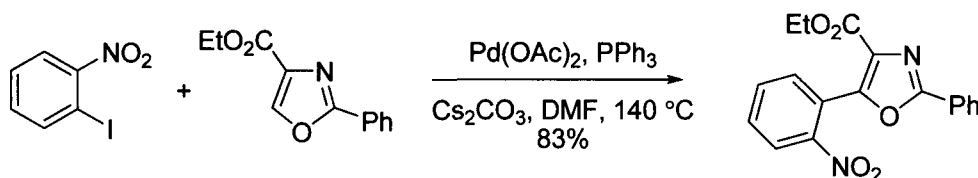
The heteroaryl Heck reaction has recently found utility in the preparation of vascular endothelial growth factor receptor-2 (VEGFR-2) inhibitors.⁹⁴ The authors proposed that inhibition of the kinase activity of VEGFR-2 would result in reduction of angiogenesis. Because tumors require angiogenesis to grow beyond a certain size, it follows that VEGFR-2 inhibition would also result in suppression of tumor growth. As such, the oxazole nucleus could be introduced onto the pyrazine scaffold under the conditions described above. The resulting molecule unfortunately displayed diminished potency in the biological assay.



The heteroaryl Heck reaction was similarly used in the preparation of potential A_{2B} adenosine receptor agonists, compounds with the potential to become a new class of drugs for the treatment of human asthma.⁹⁵



Finally, 2-iodonitrobenzene has also been effectively utilized in the heteroaryl Heck reaction to provide a fully substituted oxazole ring.⁴⁴



6.5 Selected Reactions of Isoxazoles

Reactions of isoxazoles are less prolific due to facile isoxazole ring cleavage. Isoxazoles can be treated with *N*-bromosuccinimide to brominate the C4-position of the isoxazole. In contrast to oxazoles, when an isoxazole engages in a [4 + 2] cycloaddition, the isoxazole acts as a dienophile, not a diene.⁹⁶