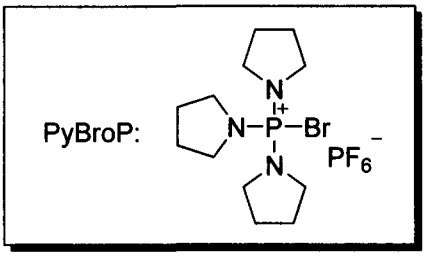
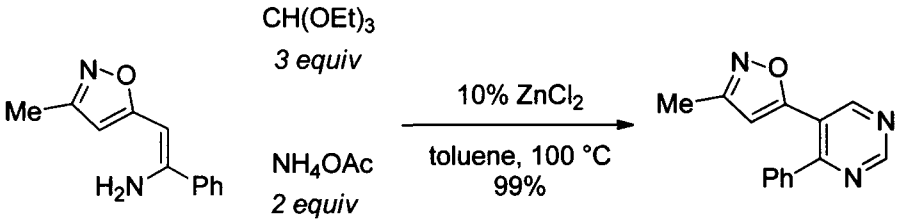


Phosphonium-based reagents PyBOP and PyBroP were found to be very effective in this transformation, affording oxytripyrrolidino-phosphonium intermediates in high yields, with PyBroP being slightly superior to PyBOP. Weak nucleophiles such as *N*-methyl benzenesulfonamide, imidazole, indole, diethyl malonate, and phenol were coupled smoothly with oxytripyrrolidino-phosphonium in high yields. *S*odium *tert*-butoxide was found to be an excellent base to ensure a clean and complete reaction.

A $ZnCl_2$-catalyzed, three-component coupling reaction involving a variety of functionalized enamines, triethyl orthoformate, and ammonium acetate, leads to the production of 4,5-disubstituted pyrimidine derivatives in a single step. This type of [3+1+1+1] annulation process has not previously been reported.[21]



13.2.3 Synthesis of Pyrimidine-Fused Systems

Movassaghi and co-workers reported a mild, convergent, and single-step procedure for the conversion of readily available *N*-vinyl and *N*-aryl amides to the corresponding substituted pyrimidines.[22] The unique reactivity associated with electrophilic activation of amides was achieved using 2-chloropyridine (2-ClPyr) in combination with trifluoromethanesulfonic anhydride (Tf_2O). Highly activated amide derivatives were trapped with weakly nucleophilic nitriles to provide the corresponding pyrimidine derivatives directly. In the process to identify the optimum reagent combination, in contrast to pyridine, 2-ClPyr was found not to add to Tf_2O. Reversible addition of nitrile and expulsion of 2-ClPyr and TfOH provided the nitrilium ion, which cyclized to pyrimidine derivatives.