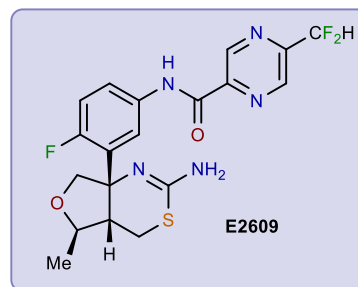
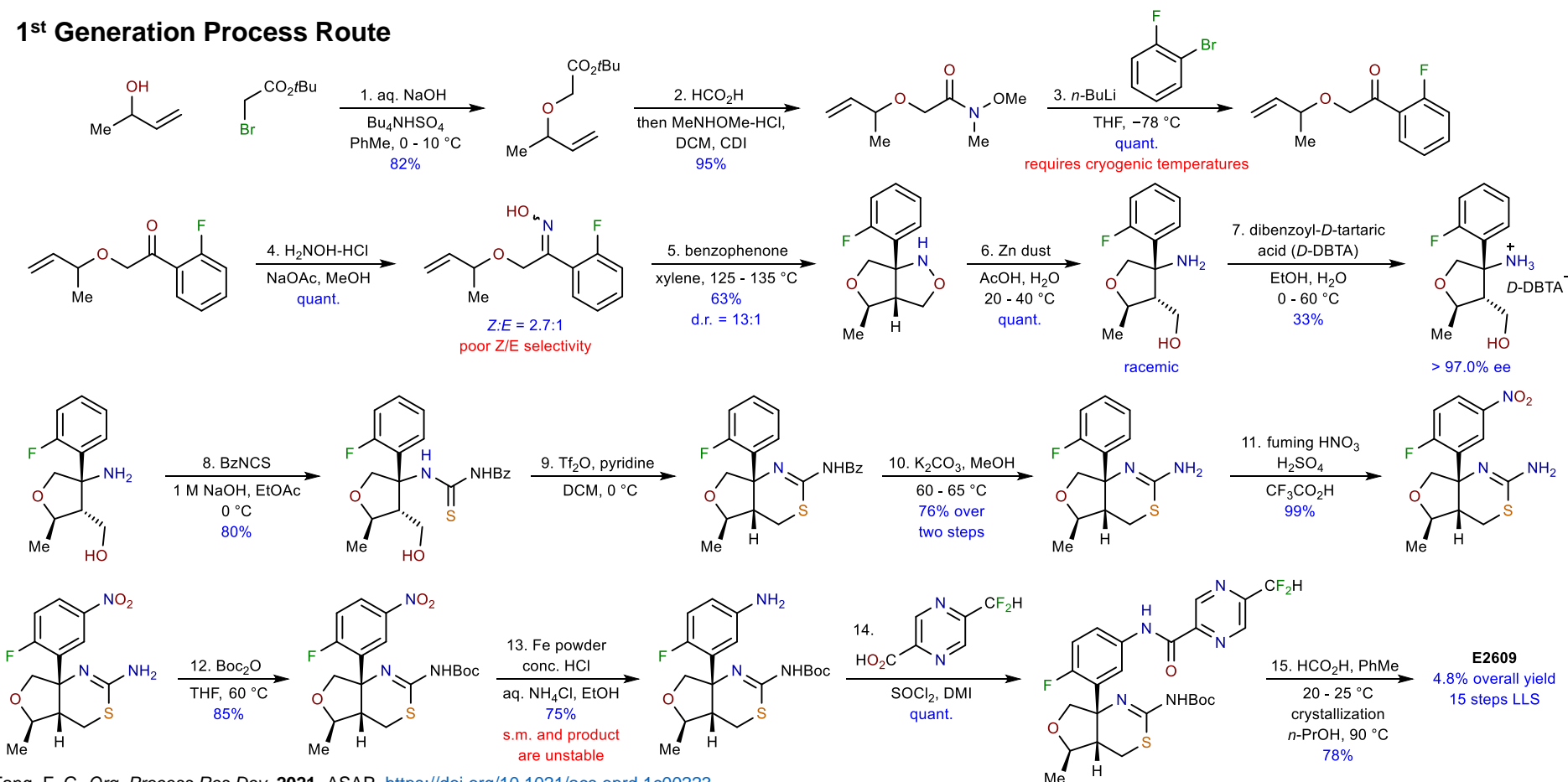


Background

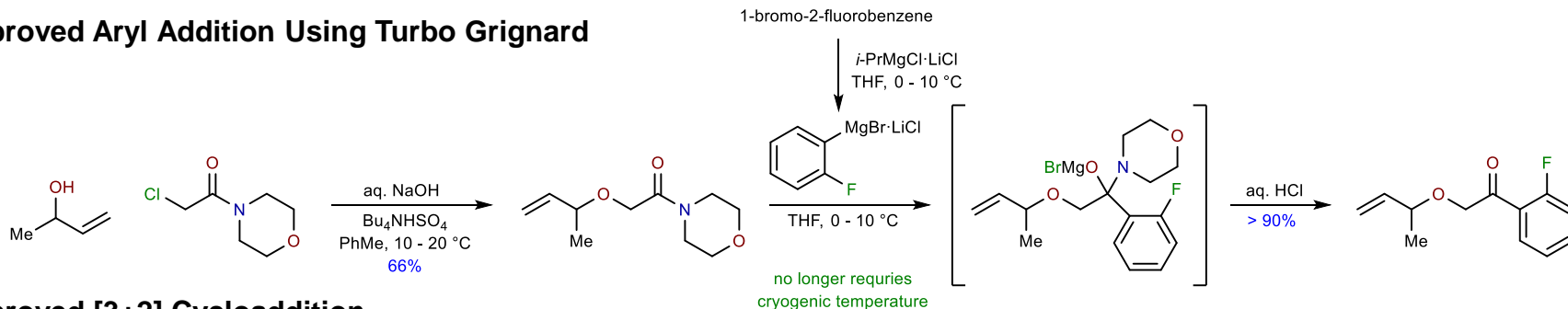
- Inhibits the beta-site amyloid precursor protein cleaving enzyme 1
 - Believed to help prevent formation of toxic beta-amyloid plaques responsible for causing Alzheimer's disease
 - As a target, BACE1 has begun to fall out of fashion due to high failure rates of lead compounds
- (See Szczepankiewicz, DOTW, 12/20/19 & Ryffel, POTW, 2/06/20)



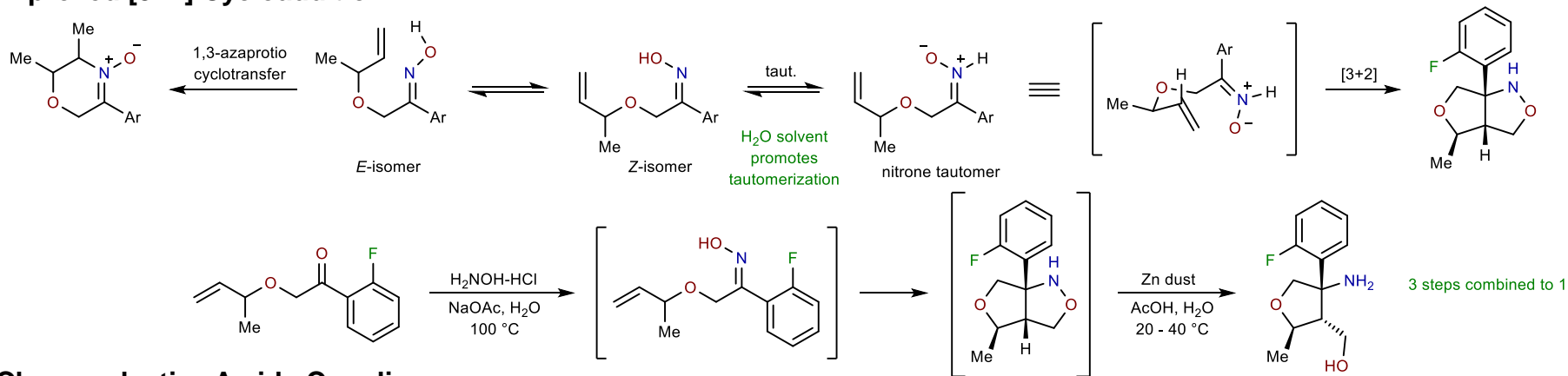
1st Generation Process Route



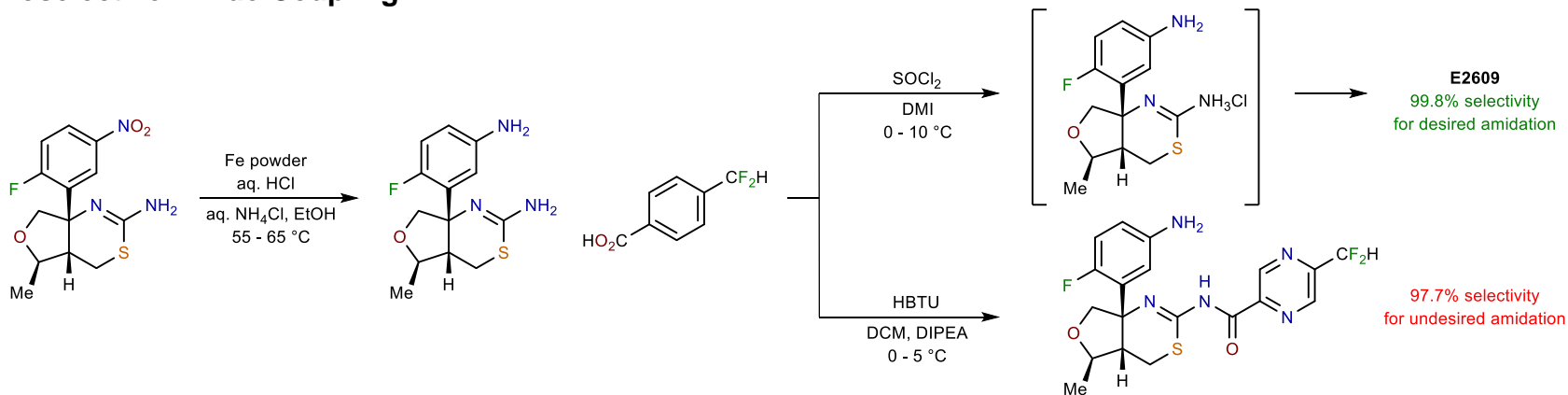
Improved Aryl Addition Using Turbo Grignard



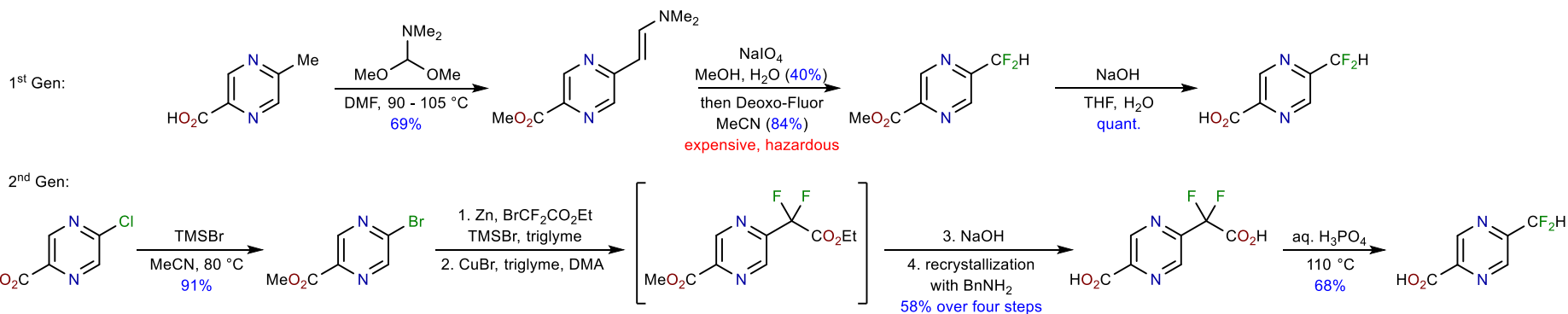
Improved [3+2] Cycloaddition



Chemoselective Amide Coupling



Reformatsky / Decarboxylation Approach for Pyrazinoic Acid



2nd Generation Process Route

