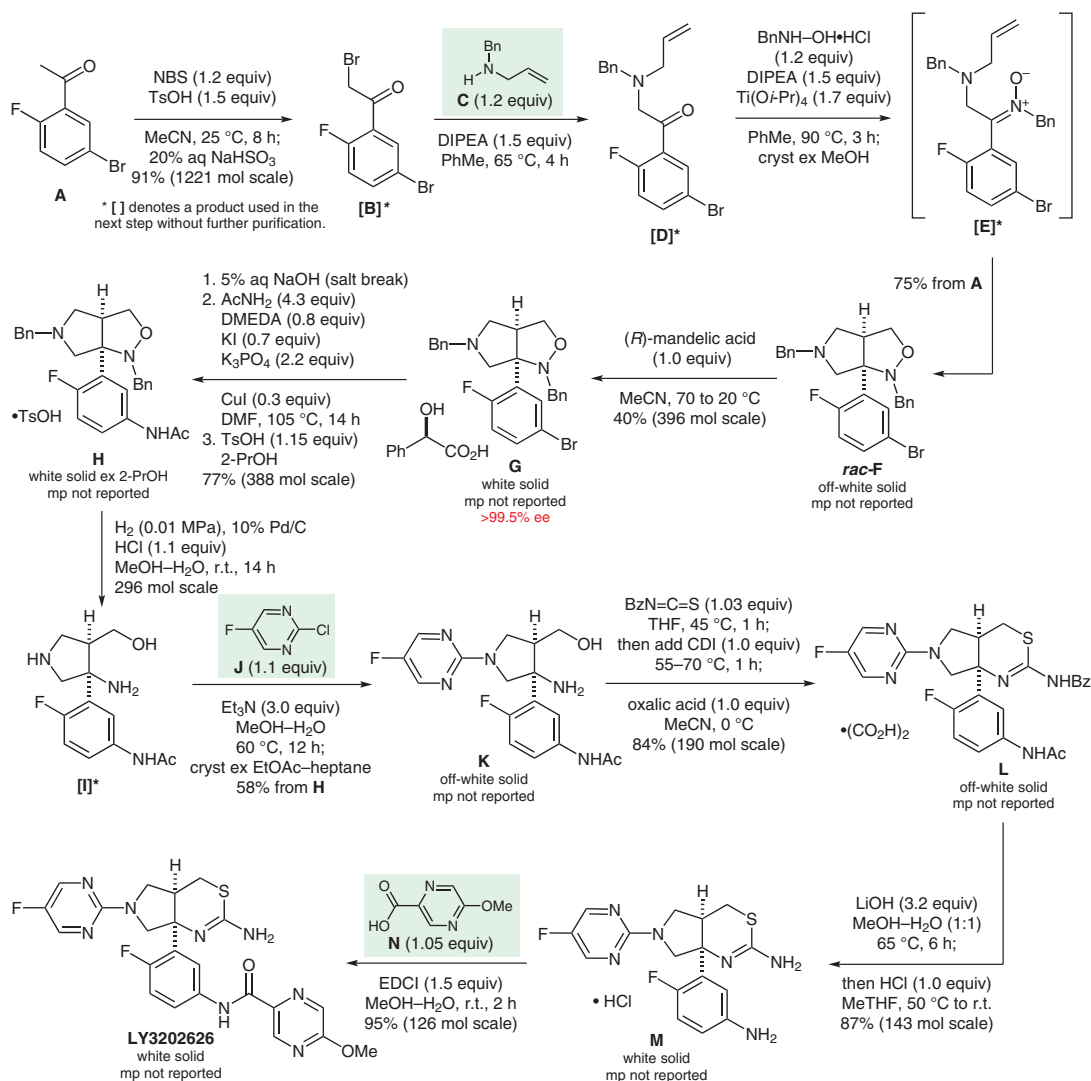


Synthesis of BACE1 Inhibitor LY3202626



Significance: LY3202626 is a beta-secretase 1 (BACE1) inhibitor that was of interest for the treatment of Alzheimer's disease. The key step in the large-scale synthesis depicted is the intramolecular [3+2] cycloaddition of nitrene **E** to give isoxazolidine *rac-F*.

Comment: The core bicyclic thiazine **L** was constructed by reaction of amine **K** with benzoyl isothiocyanate followed by cyclization of the resultant thiourea (not shown) using CDI. For the discovery synthesis of LY3202626, see: US 2014 0350245 A1.