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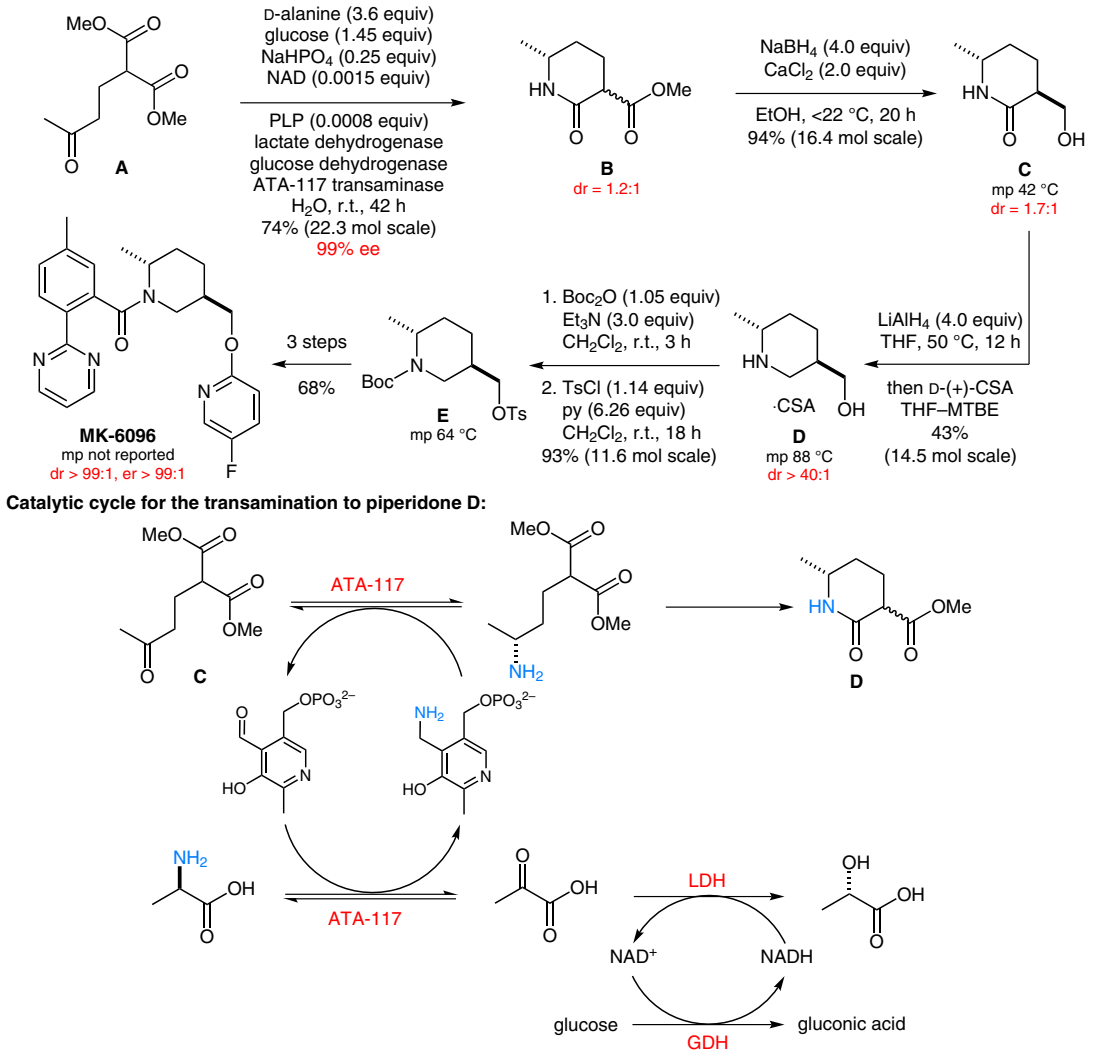
Convergent Kilogram-Scale Synthesis of Dual Orexin Receptor Antagonist
Org. Process Res. Dev. **2013**, *17*, 61–68.

Synthesis of MK-6096



Significance: The orexins are peptides that act as neurotransmitters in the central nervous system. MK-6096 is a dual orexin receptor antagonist that is a candidate for the treatment of insomnia. A noteworthy feature of the synthesis depicted is the biocatalytic transamination reaction on prochiral substrate **A** using a three-enzyme cocktail that delivers piperidinone **B** (>99% ee) on a multikilogram scale.

Comment: The diastereoisomeric ratio of the α-hydroxymethyl lactam (dr = 1.7:1) was improved to >40:1 by reduction of the lactam followed by salt formation using D-(+)-camphorsulfonic acid [D-(+)-CSA]. For the development of transaminase ATA-117 in the manufacture of sitagliptin, see: C. K. Savile et al. *Science* **2010**, *329*, 305.

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