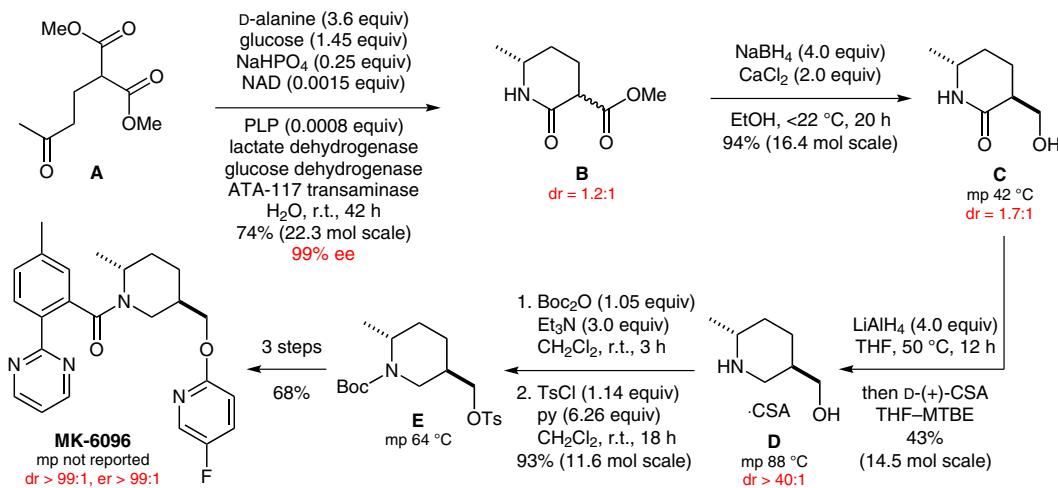
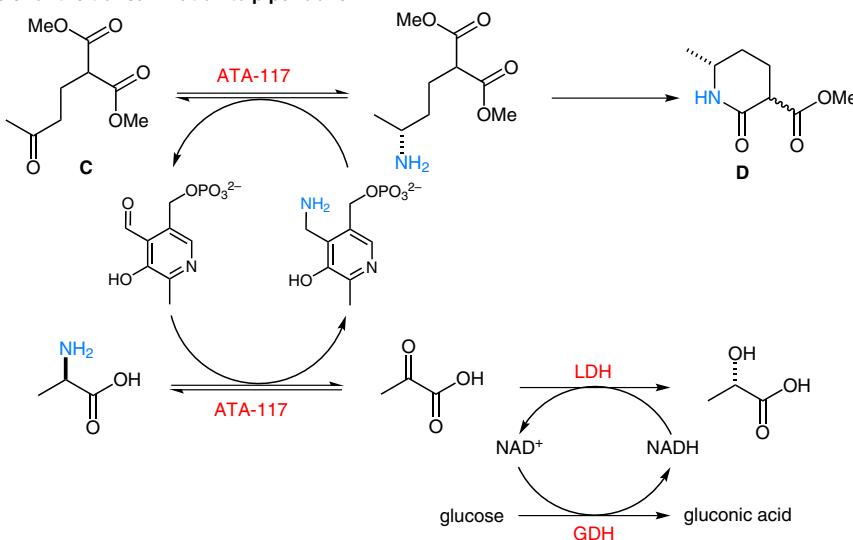


Synthesis of MK-6096



Catalytic cycle for the transamination to piperidone D:



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.

SYNFACTS Contributors: Philip Kocienski
Synfacts 2013, 9(4), 0355 Published online: 15.03.2013
DOI: 10.1055/s-0032-1318322; **Reg-No.:** K01413SF

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 sitagliptin, see: C. K. Savile et al. *Science* **2010**, *329*, 305.