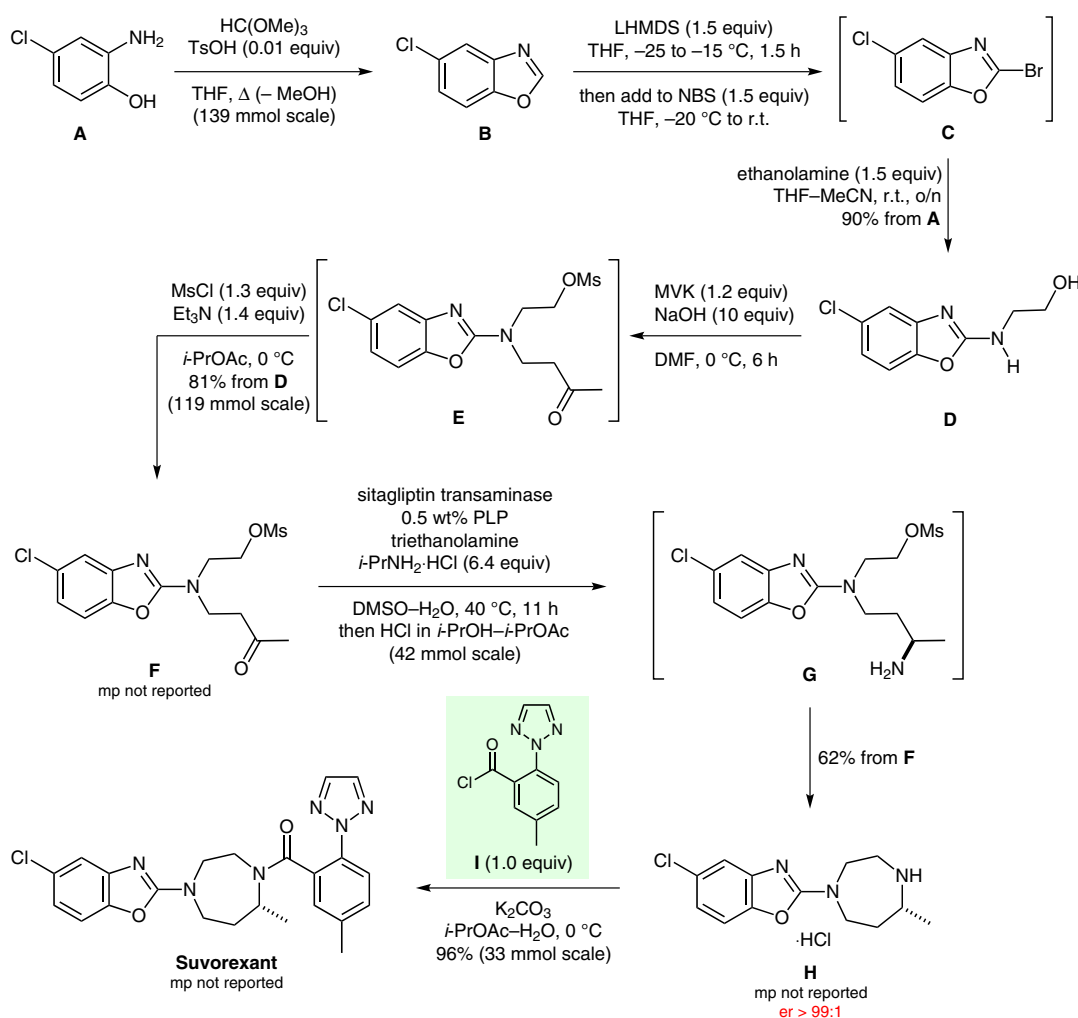


Synthesis of Suvorexant



Significance: Orexins A and B are excitatory neuropeptides that stimulate wakefulness. Suvorexant is a dual orexin receptor antagonist that is in phase III clinical trials for the treatment of insomnia. The key step in the asymmetric synthesis depicted is a tandem enzymatic transamination–annulation sequence (**F** → **G** → **H**).

Comment: A previous synthesis of suvorexant (N. A. Strotman et al. *J. Am. Chem. Soc.* **2011**, *133*, 8362) involved an asymmetric Ru-catalyzed reductive amination in the construction of the diazepane ring. The present route benefits from the circumvention of transition-metal catalysis and dichloromethane as solvent.