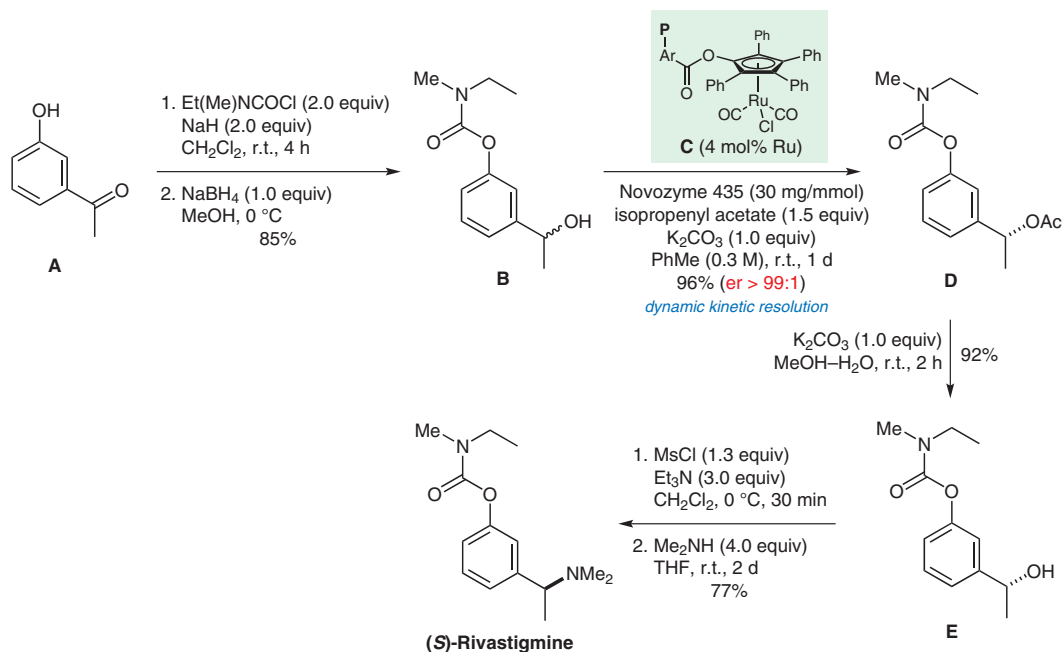


Synthesis of (S)-Rivastigmine



Significance: Rivastigmine (Exelon[®]) is an acetylcholinesterase inhibitor that is prescribed for the treatment of mild to moderate dementia in patients with Alzheimer's disease and Parkinson's disease. The key step in the synthesis depicted is a dynamic kinetic resolution of the benzylic secondary alcohol **B** involving a lipase (Novozyme 435) coupled with a polymer-bound racemization catalyst (**C**).

Comment: The polymer-bound racemization catalyst **C** was prepared by heating a polymer-bound benzoyl chloride with $[\text{Ph}_4(\eta^4\text{-C}_4\text{CO})\text{Ru}(\text{CO})_3]$ in toluene for one day. The catalyst can be recycled several times. The enzymatic resolution was performed on a 1 mmol scale. For an alternative chemoenzymatic synthesis of rivastigmine, see: J. Mangas-Sánchez et al. *J. Org. Chem.* **2009**, *74*, 5304.