**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 [Ph₄][η⁵-C₅CO]Ru(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.

**Procedure:**
1. Et(Me)NCOCl (2.0 equiv) NaH (2.0 equiv)
   CH₂Cl₂, r.t., 4 h

2. NaBH₄ (1.0 equiv)
   MeOH, 0 °C
   85%

**Novozyme 435 (30 mg/mmol)**
3. NaBH₄ (1.0 equiv)
   MeOH, 0 °C
   96% (er > 99:1)

**K₂CO₃ (1.0 equiv)**
4. isopropenyl acetate (1.5 equiv)
   K₂CO₃ (1.0 equiv)
   PhMe (0.3 M), r.t., 1 d
   96%

**C (4 mol% Ru)**
5. Novozyme 435 (30 mg/mmol)
   PhMe (0.3 M), r.t., 1 d
   96%

**K₂CO₃ (1.0 equiv)**
6. MeOH-H₂O, r.t., 2 h
   92%

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