FLUVASTATIN (LESCOL®)

Background:

- First purely synthetic HMG-CoA reductase inhibitor
  - IC_{50} = 8 nM

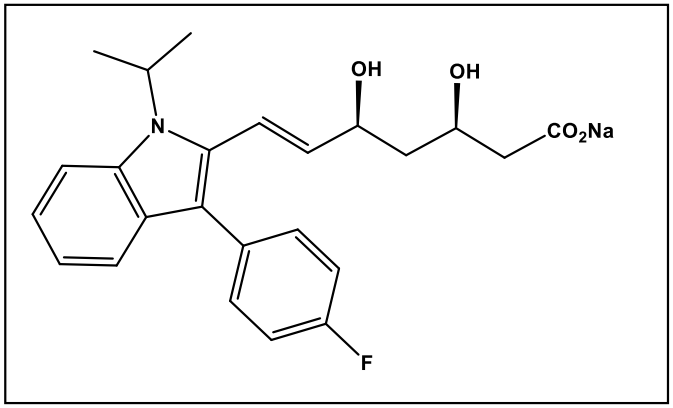
- Also inhibits hepatocyte cells
  - IC_{50} = 52 nM

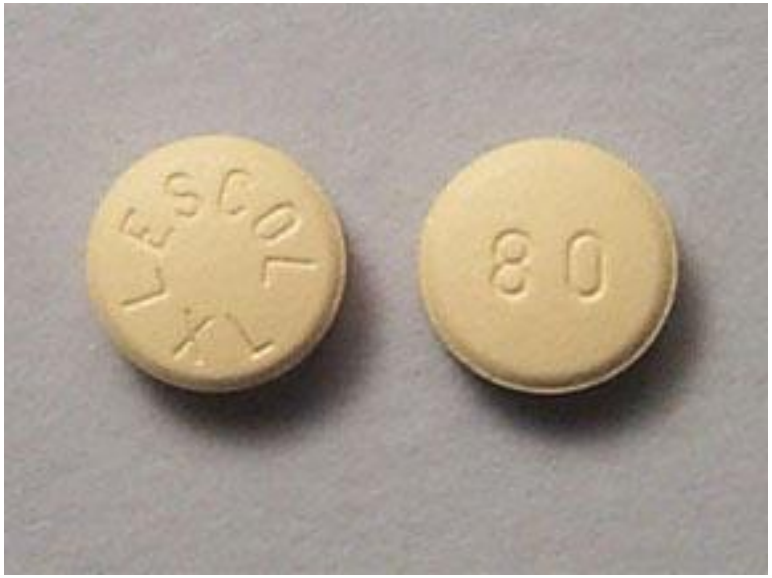
- Used for the treatment of high cholesterol

- Introduced by Novartis in 1994

- Less frequently prescribed compared to other cholesterol treatment drugs

- Prescribed as the racemate potassium salt

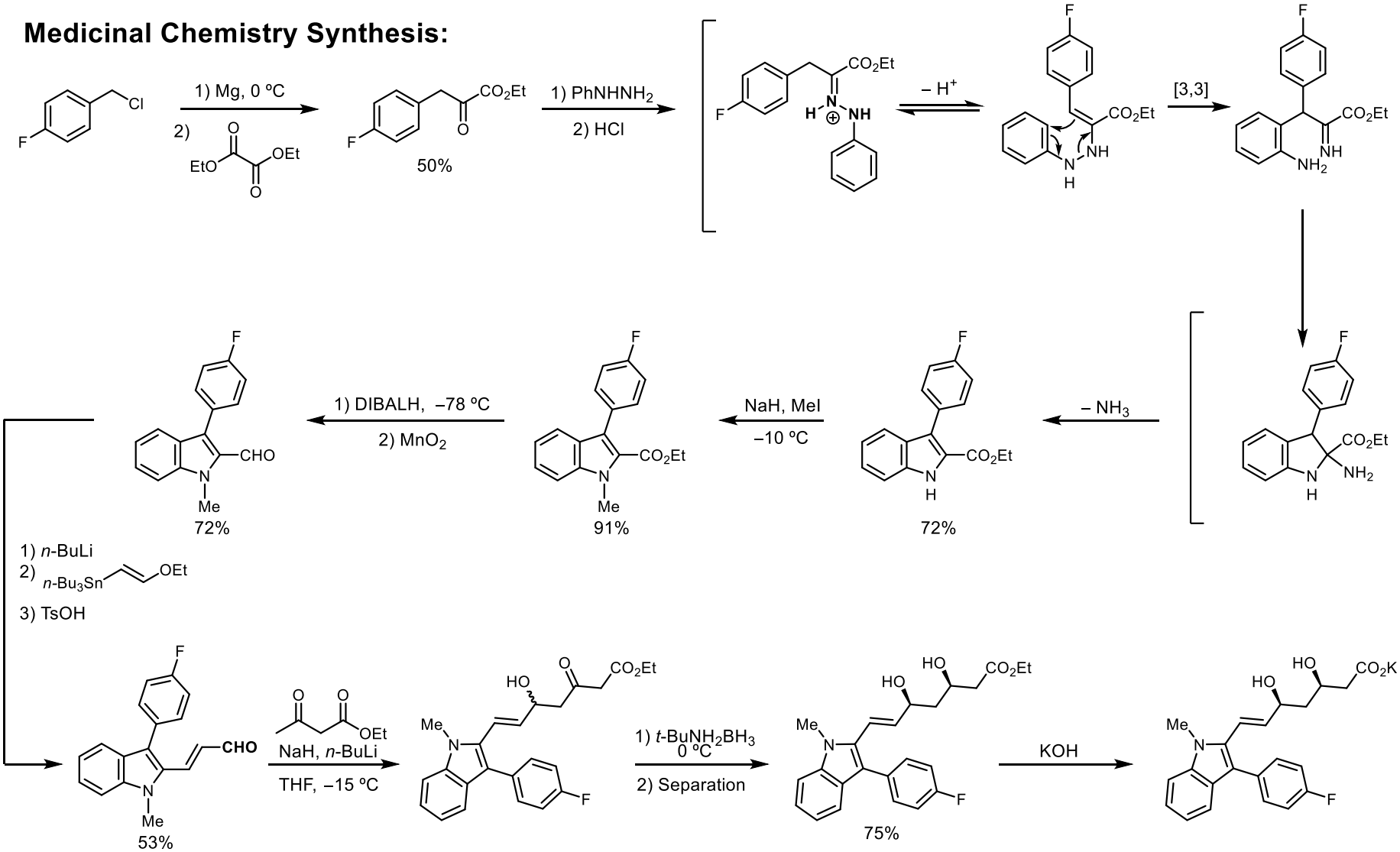




Pfefferkorn, J. A. (2007) Second-Generation HMG-CoA Reductase Inhibitors, in The Art of Drug Synthesis (eds D. S. Johnson and J. J. Li), John Wiley & Sons, Inc., Hoboken, NJ, USA.
Image from: http://www.webmd.com/drugs/2/drug-20133/lescol-xl-oral/details#

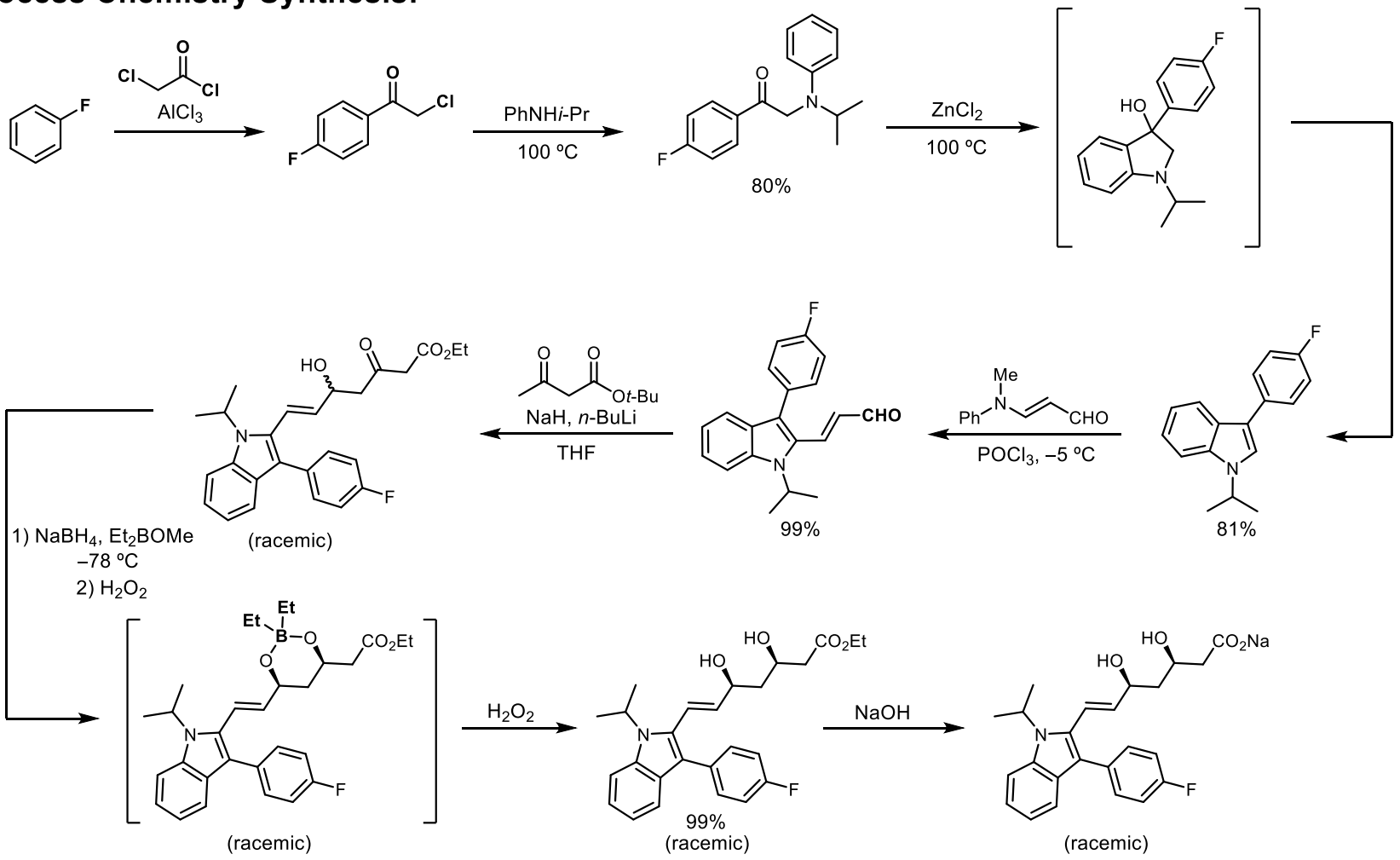
FLUVASTATIN (LESCOL®)

Medicinal Chemistry Synthesis:



FLUVASTATIN (LESCOL®)

Process Chemistry Synthesis:

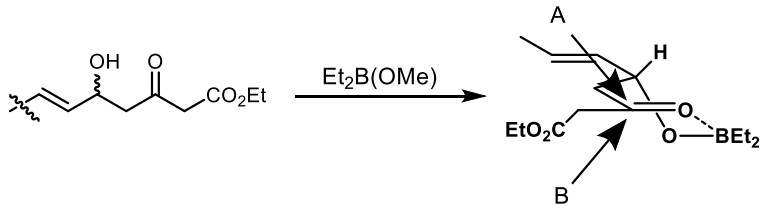


FLUVASTATIN (LESCOL®)

Improvements from med. chem. route:

- Fewer overall steps
- Obviates the need for toxic tin reagent
- *t*-Bu ester more resistant against lactonization
- Improved stereocontrol *via* chelation
- Less frequently prescribed compared to other cholesterol treatment drugs
- Prescribed as the racemate potassium salt

Chelation controlled reduction:



Path A goes through a chair-like TS,
while path B goes through a twist-boat TS