This is a key intermediate in the synthesis of the natural product aspidophyline: not a drug, but important all the same.

Problem: how to generate this chiral center when no steric bulk is around on either side

conjugate addition and elimination of OMe (see also levofloxacine)

cBS reduction uses bulk of Br to direct incoming reagent

free radical dehalogenation removes the Br directing group

esterification
\( \alpha \)-position of a carbonyl = easily installed using Evans' methodology

Naproxen (long lasting NSAID pain reliever)

weak base for selective deprotonation of phenol

Evans' chiral auxiliary installation, use for directing an alkylation, and removal

condensative heterocycle formation

deprotection and imine formation in one pot
Levofloxacin / LVX (fluoroquinolone class antibiotic used against antibiotic-resistant infections)

Conjugate addition of amine, elimination of OEt (draw the mechanism)

Aldol condensation

Three consecutive nuc. arom. substitutions, each under stronger conditions as the ring becomes less and less electrophilic due to decreasing numbers of electron withdrawing F atoms.

Atomoxetine / Strattera (norepinephrine reuptake inhibitor for treatment of ADHD)

Asymmetric epoxidation

Reduction opens least hindered side of epoxide

Mitsunobu rxn - you haven't learned this, but the key is that it goes with perfect inversion
This synthetic intermediate is used to make haplophytine, another natural product, that is a natural insect repellant.

**key issues: how to construct these heterocycles**

Friedel-Crafts acylation: a reliable way to make aryl-carbon bonds

this works on both carbonyls because one is an amide, and the other is a very electron-rich ketone: you could have use other reductants

A Pictet-Spengler reaction stitches this heterocycle together

Avandia (treatment of type II diabetes by reducing insulin resistance)

This drug is racemic, so the key problems are simple linkages

another nuc. arom. subs... yes, the carbonyl is electron-withdrawing enough to allow the attack onto this fluorobenzene ring

epoxide opening

nuc. arom. subs.

Avandia

NaOEt, removal of water

H₂, Pd/C