Problem Set May 2008 – Retrosynthesis

In this problem set we will start by revising the disconnection approach to organic synthesis. You will first have to propose disconnections for a few common functional groups and then we will go on to apply these principles towards the syntheses of a few pharmaceutically relevant molecules.

A Few Simple Starters

Propose disconnections and suitable syntheses for each of the following molecules 1-6. Where necessary, can you suggest ways to make the syntheses enantioselective?

![Molecules 1-6](image1)

Some Heterocyclic Chemistry

Thanks to James we have seen plenty of heterocyclic chemistry before. Here are a few more examples which should help to prepare you for tackling the syntheses of the drug-like molecules to come. How would you synthesize compounds 7-10 from acyclic precursors?

![Compounds 7-10](image2)

Synthesis of Pharmacologically Active Compounds

Now to finish off by looking at some drug molecules; can you suggest feasible syntheses for the following marketed compounds?
Delavirdine Mesylate, Rescriptor®

Delavirdine is a member of the bis(heteroaryl)piperazine class of HIV-1 reverse transcriptase inhibitors. It is administered orally as its mesylate salt and was launched by Pfizer under the name Rescriptor® in 1997.

Aprepitant, Emend®

Aprepitant is orally administered to help alleviate the nausea commonly associated with cancer chemotherapy. It was developed by Merck and was the first commercially available neurokinin NK-1 antagonist.