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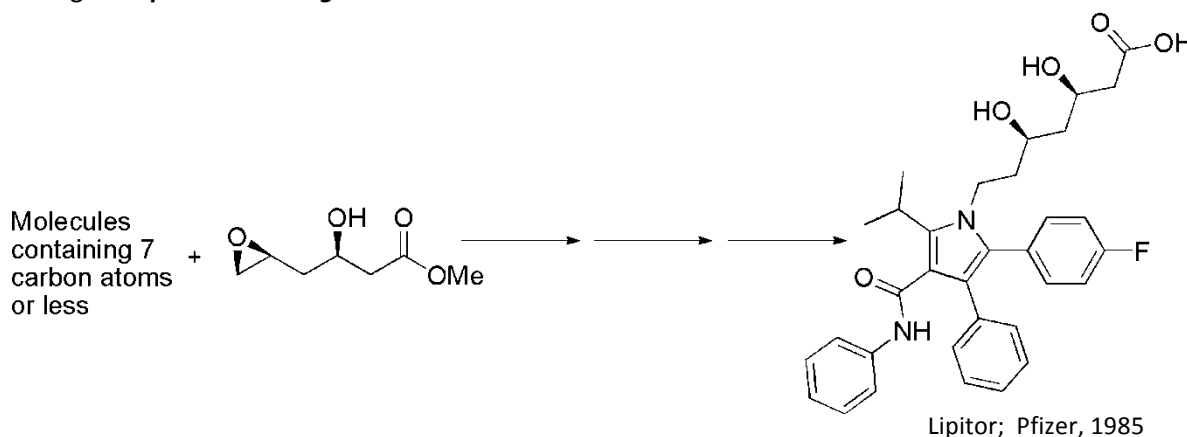
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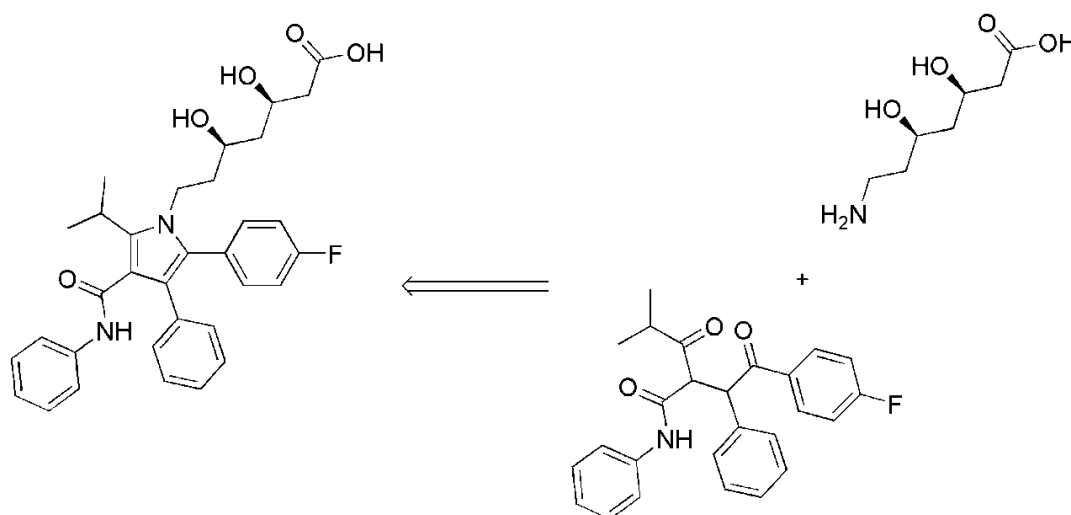
PS #9 – Planning the Synthesis of a Complex Target Containing a Heterocyclic Core

Part A) Lipitor (Pfizer) is the number one selling drug in the world, with 2006 sales of US\$12.9 billion. It was first synthesized by Bruce Roth in 1985 when he was with Pfizer. He was later named the 2008 Hero of Chemistry by the American Chemical Society. The patent on Lipitor is due to expire in 2010. Create your own synthesis of generic Lipitor. A good synthetic route is one that is efficient, cheap and direct and, if it's really good, one day you could be a Hero of Chemistry too.

The pyrrole heterocycle can be generated via condensation. Before proposing a synthesis, disconnect the pyrrole ring into two reasonable fragments. As a group, design a synthesis of Lipitor based on the disconnection of the pyrrole ring. You may use **any molecules containing 7 carbon atoms or less**, including the **epoxide starting material** below.

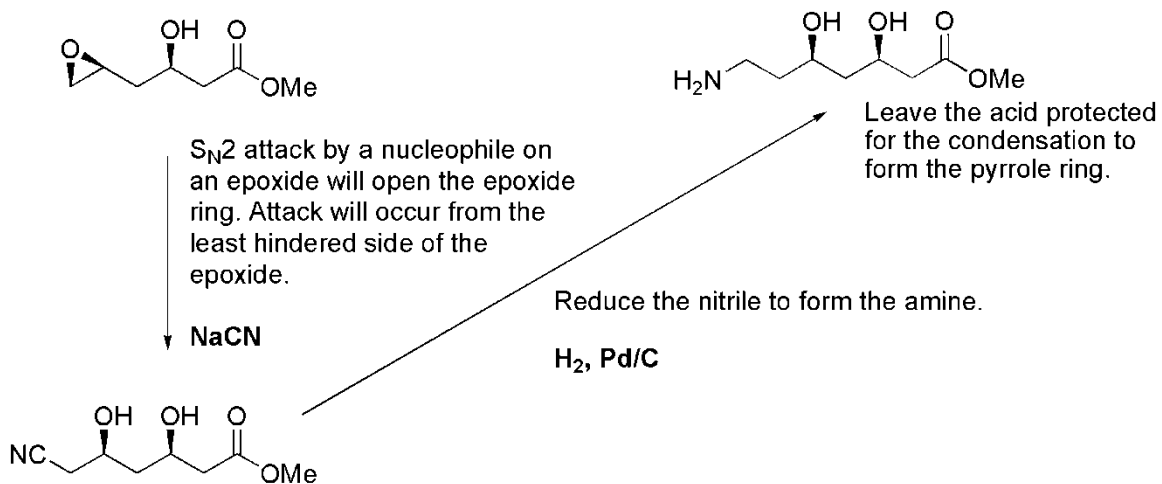


One way pyrrole rings are synthesized is by condensing diketones with amines. The pyrrole ring in Lipitor can be disconnected to give the following two fragments.

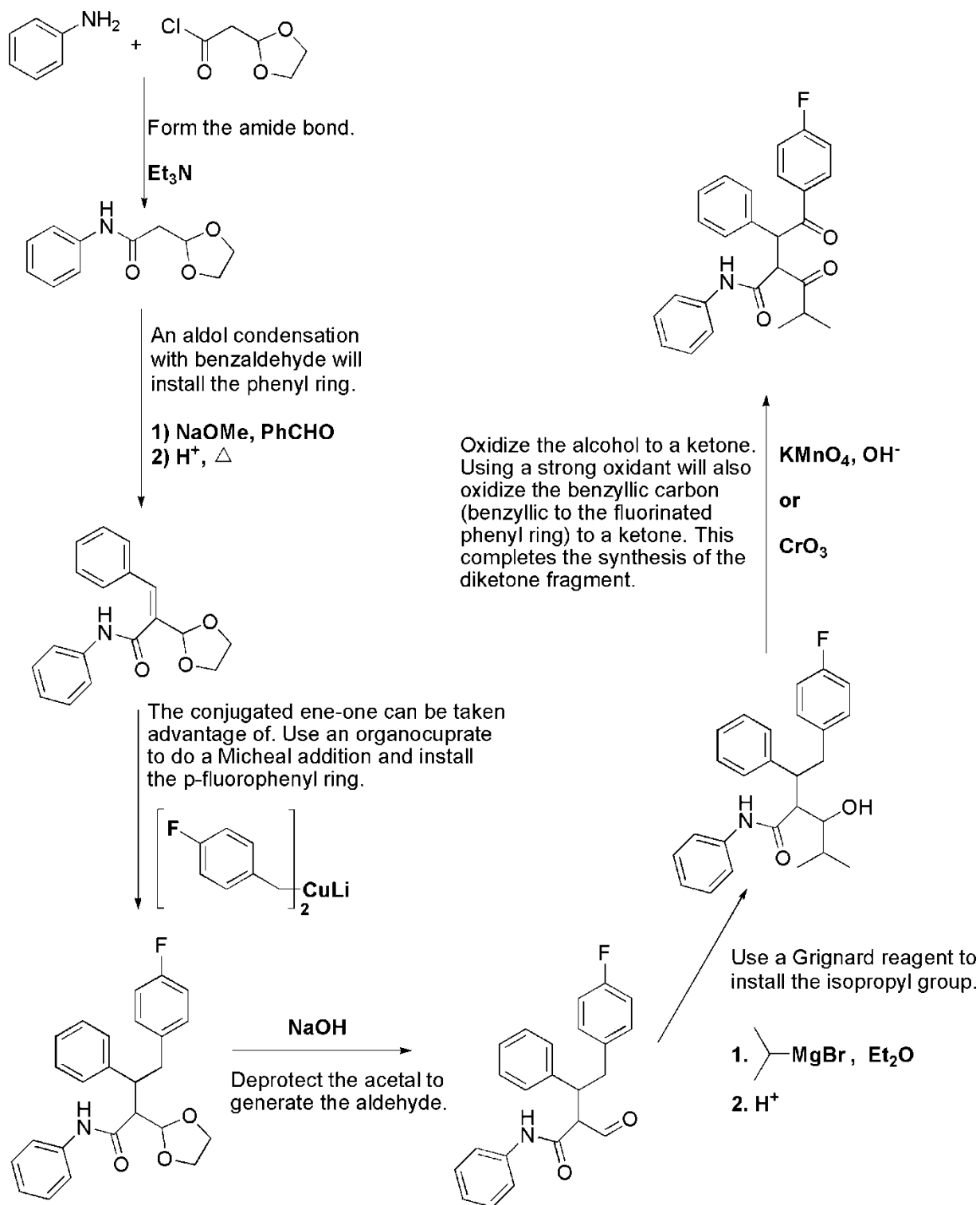


Now synthesize each fragment. Note that the carboxylic acid in the amine fragment will have to be protected prior to condensation with the diketone.

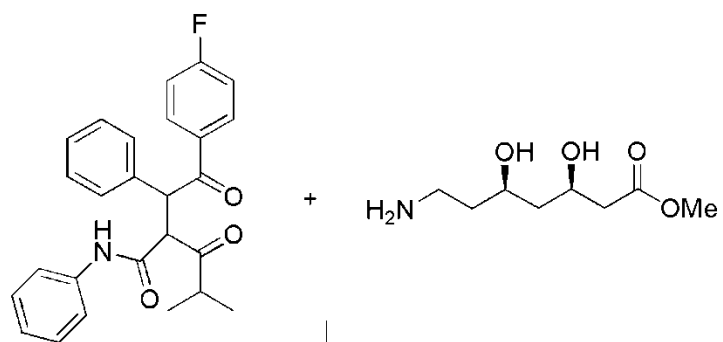
Synthesize the amine fragment. The epoxide starting material provided will generate the product with the correct stereochemistry (*R,R*).



Synthesize the diketone fragment.

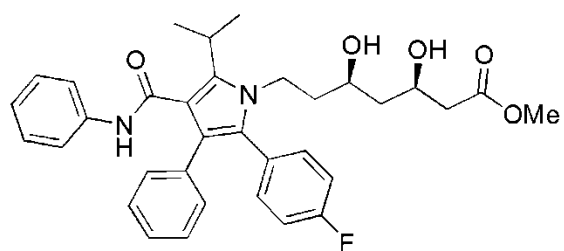


Condense the two fragments and hydrolyze the ester to give Lipitor.



Use a non-nucleophilic
base for the condensation.

Pyridine



Hydrolyze the ester.

1. NaOH, H₂O
2. H⁺

