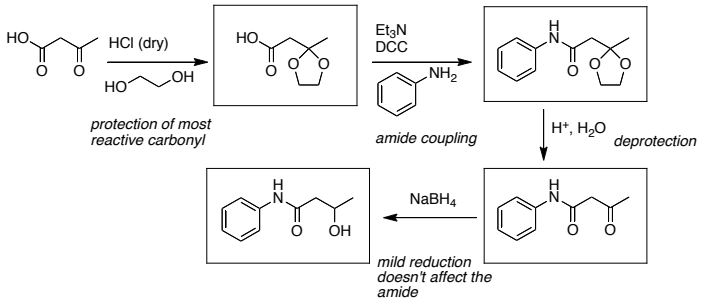
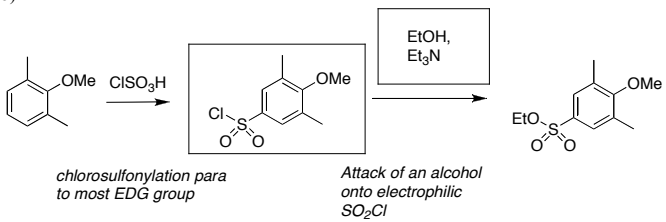
2010 — Problem set 2 ANSWERS
Chapter 25.

1) Fill in the missing products and reagents/conditions where needed.

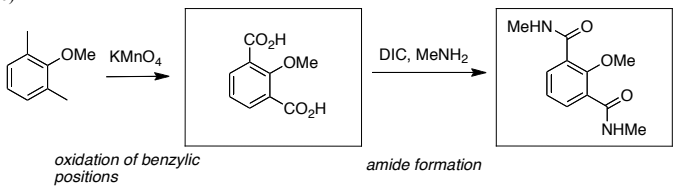
a)



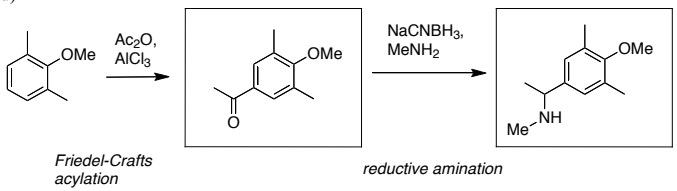
b)



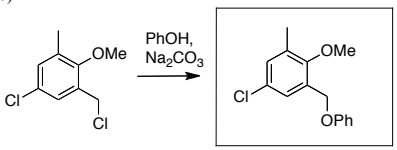
c)



d)

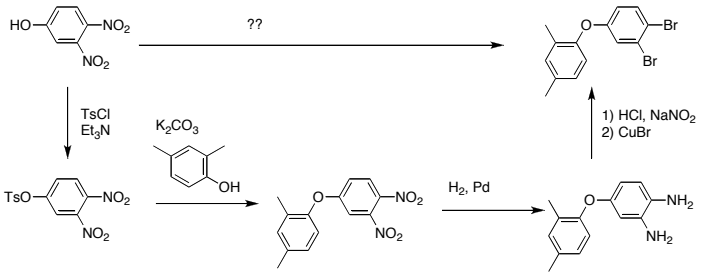


e)

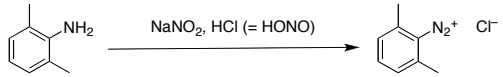


The ring Cl is not a leaving group... this is an electronic rich ring!

2) Plan the following multi-step synthesis. Do not show mechanisms.



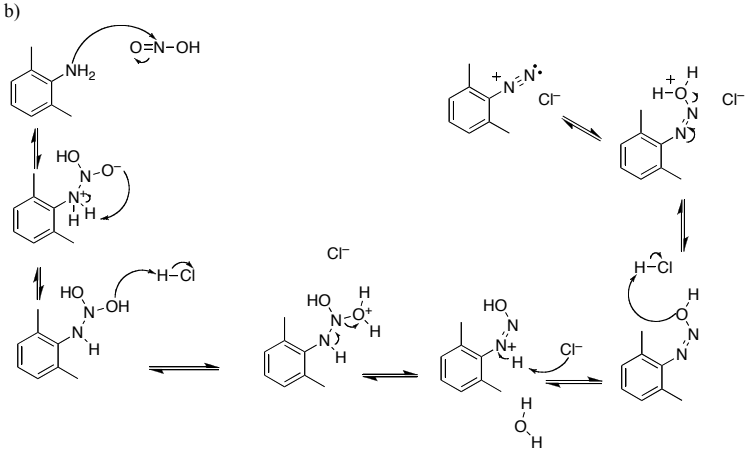
3) Consider the following transformation.



a) Draw the product diazonium in full, unabbreviated form that shows all lone pairs and bonds.
b)Give the mechanism of the following transformation. Show all proton transfers, intermediates, and byproducts.
c) What byproducts are produced? Is this reaction catalytic in H^+?

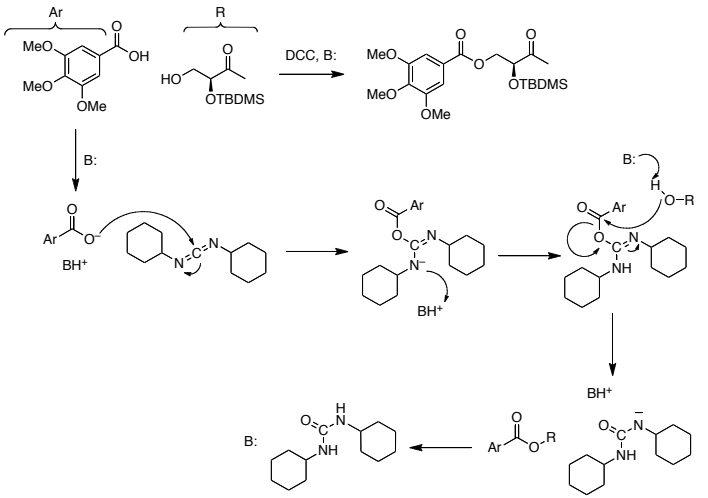
a)

b)



c) There are two equivalents of water produced. The reaction consumes one equivalent of H^+.

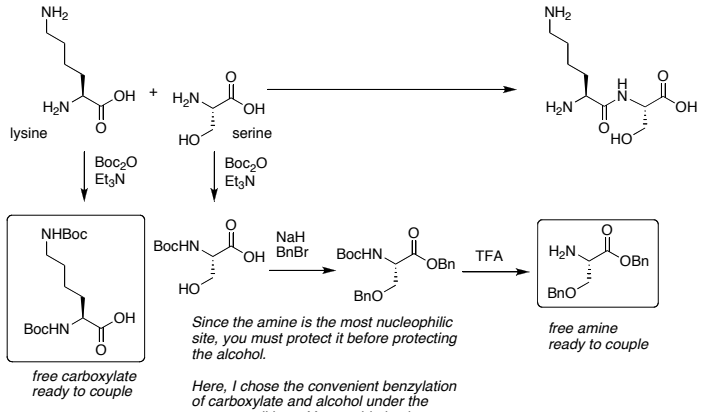
4) In addition its usual role in peptide synthesis, dicyclohexylcarbodiimide (DCC) is routinely used for mild ester formation on complex substrates. Draw the detailed mechanism of this transformation, tracking all proton transfers carefully. Is the reaction catalytic in DCC? Is the reaction catalytic in Base?



The DCC is converted to dicyclohexyl urea... so it is not a catalyst.
The original equivalent of base is regenerated by the end of the reaction, so it is a catalyst.

5) Amino acid *side chains* can also have functional groups that need to be protected during synthesis.

For the coupling shown below, create a derivative of *each* amino acid monomer that is suitably protected in order to undergo the coupling shown. Show in detail how each amino acid could be converted to its protected form. Include intermediates, reagents, and conditions, but not mechanisms.



Since the amine is the most nucleophilic site, you must protect it before protecting the alcohol.

Here, I chose the convenient benzylation of carboxylate and alcohol under the same conditions. You could also have protected them independently, but at the cost of extra steps (and likely a couple of marks)