Chemistry 224
Bioorganic Chemistry
Exam 1

Name _____
Friday, Sept. 29, 2000
100 points

This Exam is closed book and closed notes

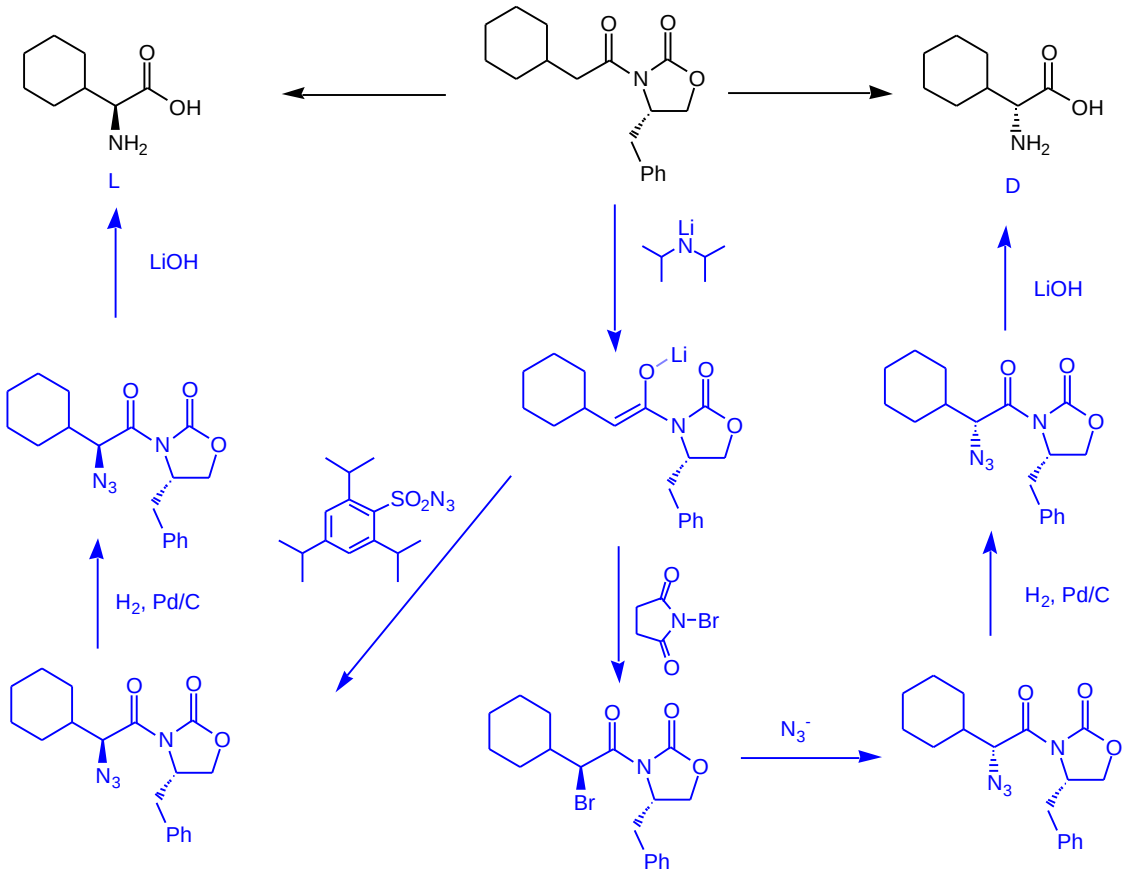
Please show all your work!

Stereochemistry counts as indicated!

Neatness counts!

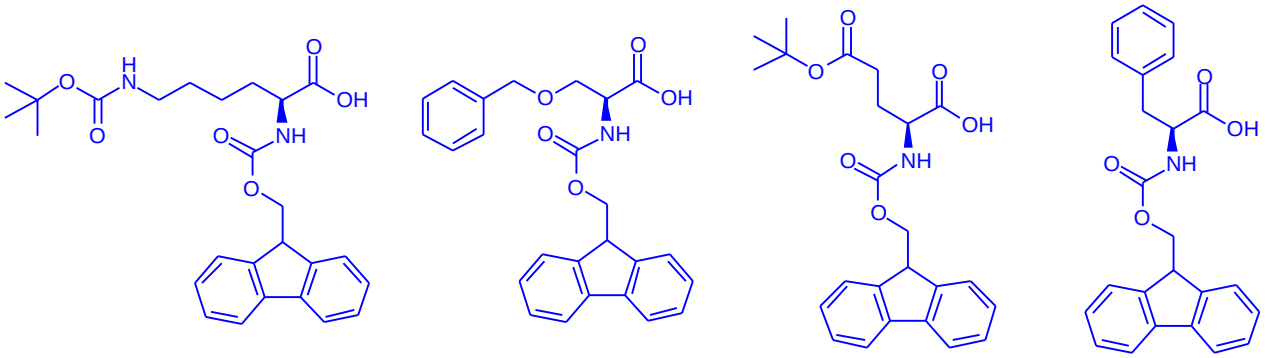
Good Luck!!

1. The amino acids shown below are more hydrophobic analogues of valine. Both enantiomers can be prepared from a common chiral oxazolidinone precursor shown below. Provide all reagents and show all intermediates for the synthesis of both enantiomers. Also, label the amino acid products as either the D- or L-enantiomer. (12 pts)

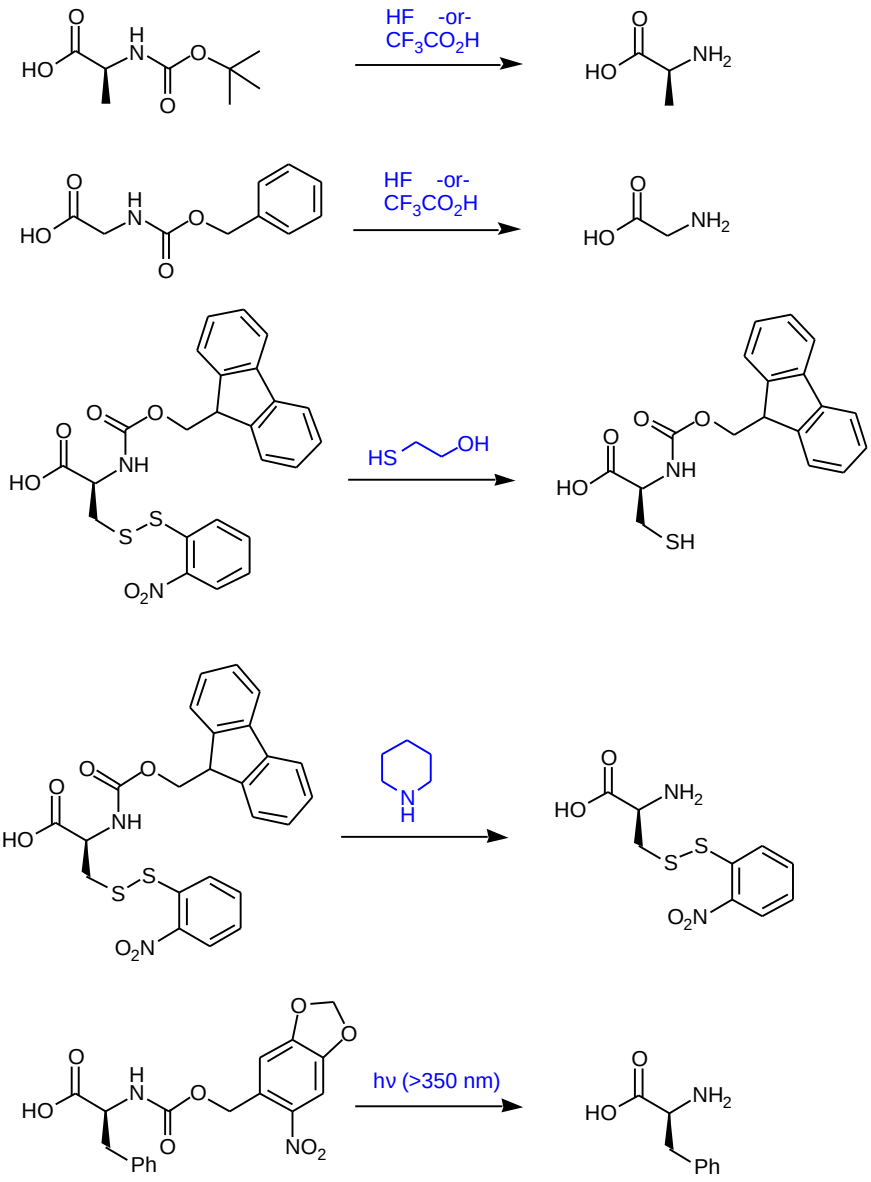


2. Draw suitable reagents for incorporation of the following amino acids using solid phase peptide synthesis. Do not abbreviate any part of the structure unless you have already drawn it once. (12 pts)

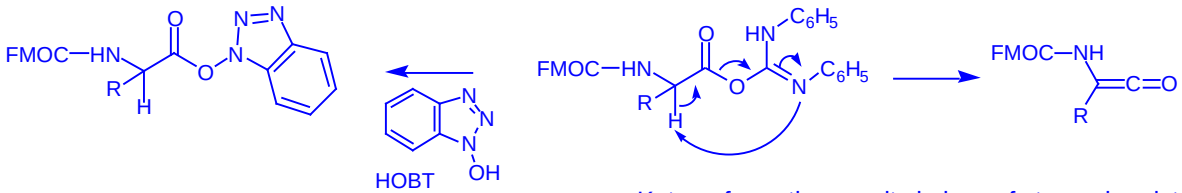
a. lysine b. serine c. glutamic acid d. phenylalanine



3. Provide reagents for the following deprotection reactions (15 pts):



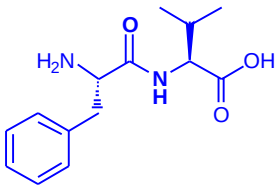
4. Using dicyclohexylcarbodiimide (DCC) alone for the amide bond forming step is often unsatisfactory for peptide synthesis. Briefly explain why, show how the troublesome process occurs and what is done to circumvent the problem. (10 pts)

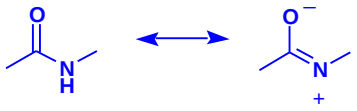


HOBT ester does not under ketene formation. Amide formation can occur without stereochemical scrambling

Ketene formation results in loss of stereochemistry (scrambling) of the α-carbon. When this couples with an amino group to form an amide, diastereomers are formed

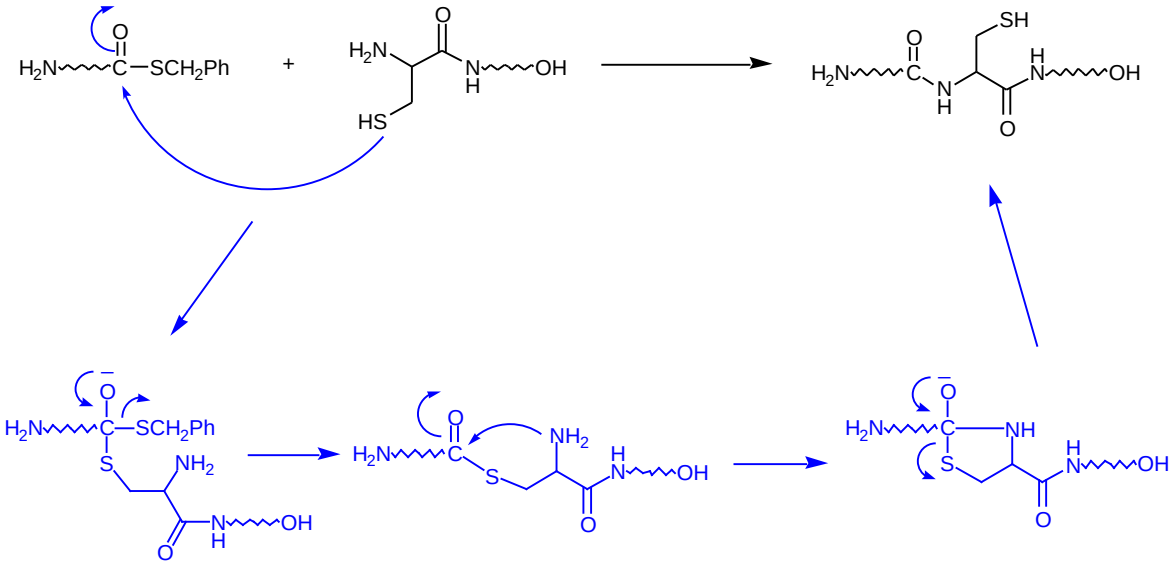
5. Draw fully (including sidechains and stereochemistry), any dipeptide using two different amino acids. Identify and indicate the hybridization of all the atoms involved in the amide bond. Briefly explain why this bond has enhanced stability. (10 pts)





C, N, O of the amide
are all sp2 hybridized

6. A large peptide (or protein) can be synthesized by joining together two smaller peptides. This is known as a convergent peptide ligation. Give the mechanism for this process. Show only the relevant portions of the peptides. (10 pts)



7. Consider the following peptide.

SER-TYR-PRO-ASP-GLN-LEU-GLY-LYS-VAL-CYS-MET-ILE-GLU-SER-LEU-SER-THR-VAL

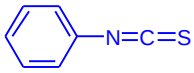
a. The peptide was treated with cyanogen bromide (BrCN), then sequenced by Edman degradation. Show where cyanogen bromide will cleave the peptide (3 pts).

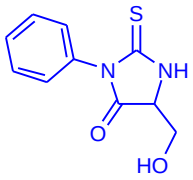
SER-TYR-PRO-ASP-GLN-LEU-GLY-LYS-VAL-CYS-MET-ILE-GLU-SER-LEU-SER-THR-VAL

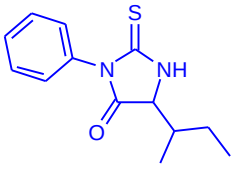
b. When the two fragments are sequenced, how do you know which fragment is from the C-terminal and N-terminal ends of the original peptide (3 pts).

The N-terminal fragment of the original peptide will have a C-terminal homo-serine residue (from the cyanogen bromide cleavage of methionine), which is an unnatural amino acid that can be readily identified by Edman degradation

c. What is the reagent used for Edman degradation? For either fragment, draw the structure of the first product from Edman degradation. (3 pts)



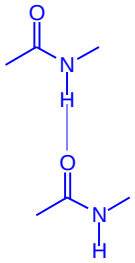




d. When the peptide is sequence by mass spectrometry, two of the fragments show a mass loss of 128, which could be either lysine (LYS) of glutamine (GLN). How can these amino acids be differentiated when sequenced by mass spectrometry? (3 pts)

The sidechain amino group of LYS will react with acetic anhydride to for an acetyl group. The derivatized fragement will have a mass of 128 + 42 (for the acetyl group). GLN does not react with acetic anhydride. After reaction with acetic anhydride, the MS sequencing is run again to see of the residue has a mass of 170 for LYS, or 128 for GLN.

8. Hydrogen bonding between amide groups is important for defining the structure of proteins. Draw a hydrogen bond between two amide groups and name one common structural motif within a protein where such hydrogen bonding is important. (7 pts)



Found in α-helix, β-sheet, β-turn

9. Combinatorial libraries are classified by how the libraries are synthesized. What are the two types of combinatorial libraries and briefly discuss the strengths and weaknesses of each. (12 pts)

Split Synthesis (mixture libraries): Can make very large libraries, however deconvolution of the mixture can be tedious

Spatially Addressable Parallel Synthesis: No need to deconvolute the libraries, since each well or pin contains only one compound. These libraries tend to be significantly smaller than those from split synthesis