Chemistry 224   Name _____

Bioorganic Chemistry   Friday, Sept. 29, 2000

Exam 1   100 points

<u>This Exam is closed book and closed notes</u>

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)
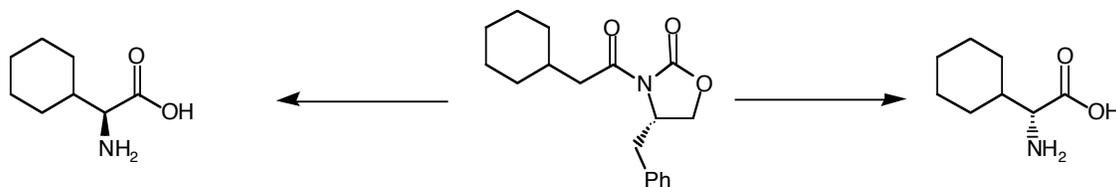
2. Draw suitable reagents for incorporation of the following amino acids using solid phase peptide synthesis. Do not abbreviate any part of the structure unless you have already drawn it once. (12 pts)
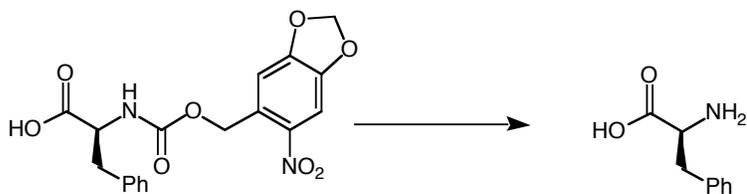
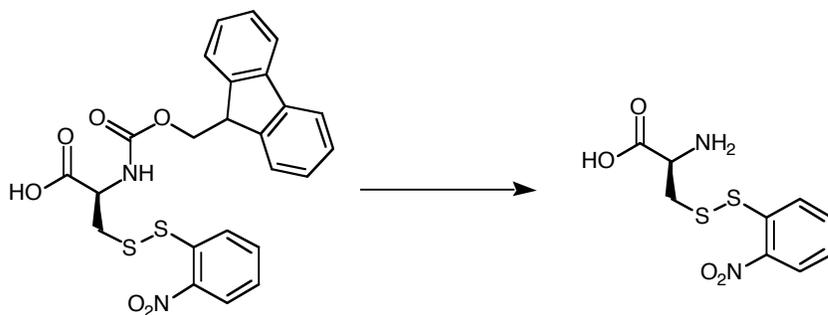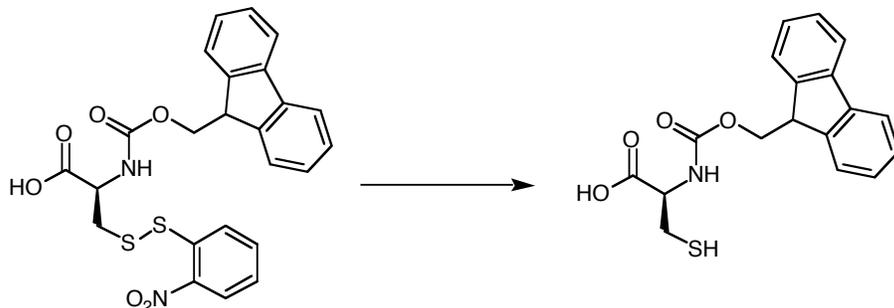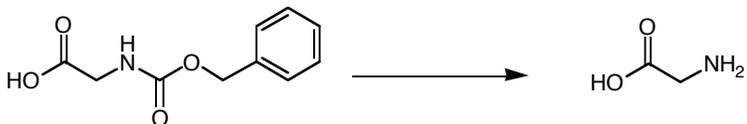   a. lysine   b. serine   c. glutamic acid   d. phenylalanine
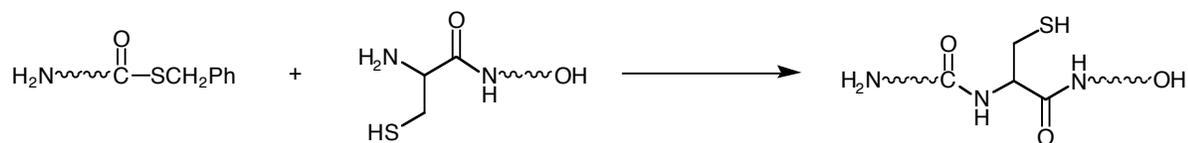
3. Provide reagents for the following deprotection reactions (15 pts):

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)

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)

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).

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).

c. What is the reagent used for Edman degradation? For either of the 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 showed 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)

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

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)