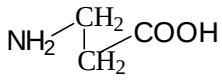
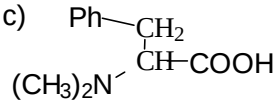
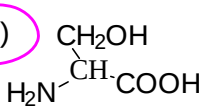
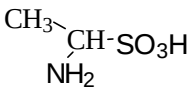
Practice Problems on Amino Acids and Peptides

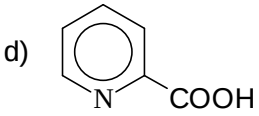
1. Which one of the following is a standard amino acid found in proteins?

a) 

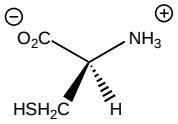
c) 

e) 

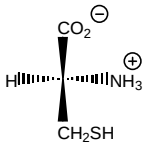
b) 

d) 

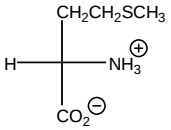
2. Which one of the following amino acids is least likely to be naturally occurring?



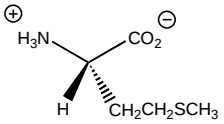
A



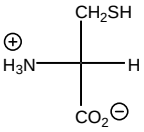
B



C



D



E

D, not L

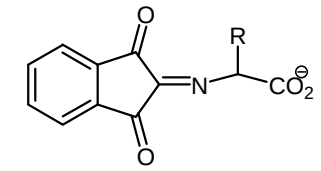
3. Amino acids are amphoteric. Which statement best describes the definition of the term *amphoteric*?

A) Amino acids exist as a zwitterion in the solid state
B) Amino acids possess both acidic and basic functional groups
C) An aqueous solution of an amino acid will conduct electricity
D) Amino acids are soluble in water
E) Amino acids are colourless

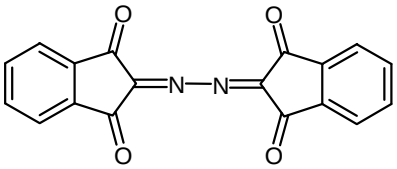
4. Ninhydrin reacts with most α-amino acids to produce a purple compound. Which structure is not reasonably involved in the formation of the compound?

write out mechanism

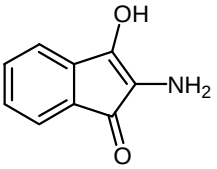
A



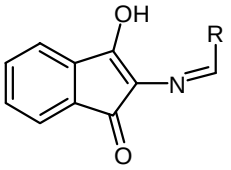
B



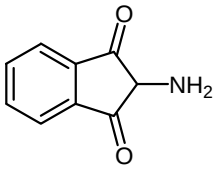
C



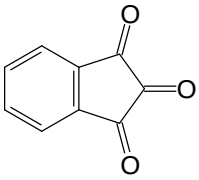
D



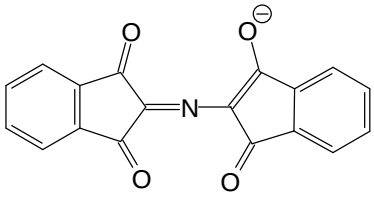
E



5. All but one of the natural amino acids react with ninhydrin (**I**) to give a purple pigment (**II**). Which one of the five listed will not react with ninhydrin to give **II**?



I



II

no 1° amine

Asp Cys Met Pro Leu

6. In order to work out the structure of a protein, a necessary first step is to analyze for the amounts of each amino acid contained in it. The amino acid analyzer developed for this purpose involves which one of the following?

A) A set of twenty specific enzymes, one to react with each amino acid, producing a characteristic color reaction.

B) Separating the amino acids by paper chromatography and then converting the spots to colored derivatives.

C) Converting the amino acids to colored derivatives and then separating them by column chromatography.

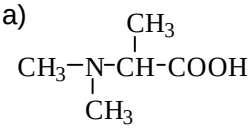
D) Converting the amino acids to colored derivatives and then separating them by paper chromatography.

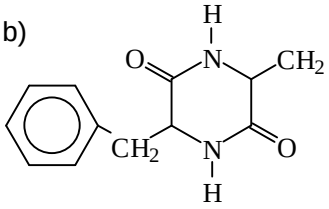
E) Separating the amino acids by column chromatography and then doing a color reaction to measure the amount of each.

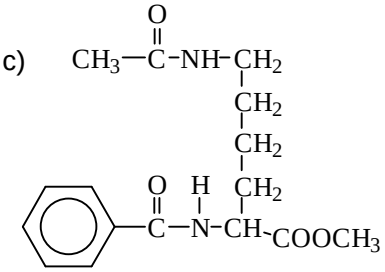
post-column derivatization

7. Which one of the following can react with Sanger's Reagent?

need nucleophilic nitrogen

a) 

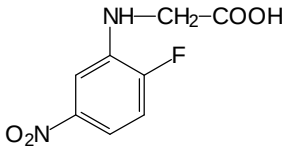
b) 

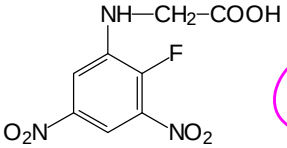
c) 

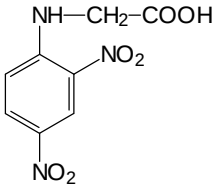
d) NH_2-CH_2-$COOCH_3$ e) CH_3-CO-NH-CH_2-COOH

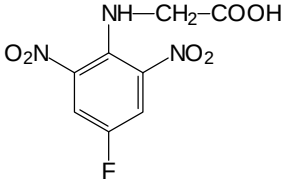
3° and amide nitrogens are not nucleophilic

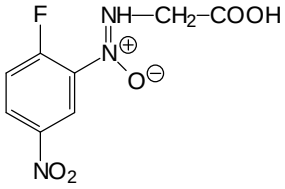
8. What is the structure of the product formed from the reaction between glycine and Sanger's Reagent?

A 

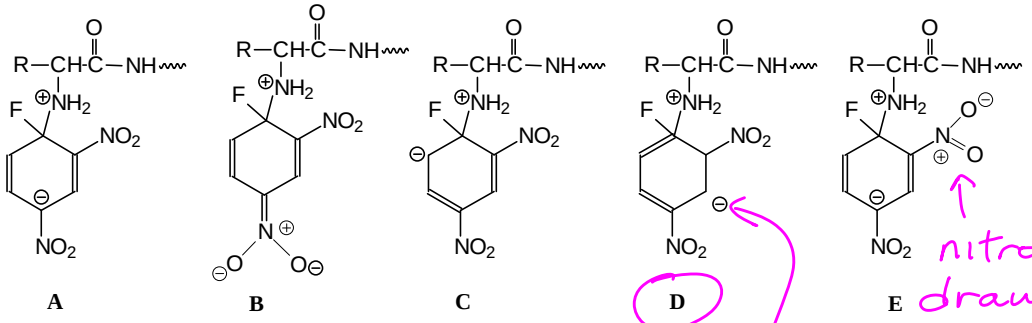
B 

C 

D 

E 

9. Which one of the following structures is *least likely* to be an important contributing structure of the intermediate formed during the reaction of Sanger's reagent (fluorodinitrobenzene) with the N-terminal amino acid of a polypeptide?



A B C D E

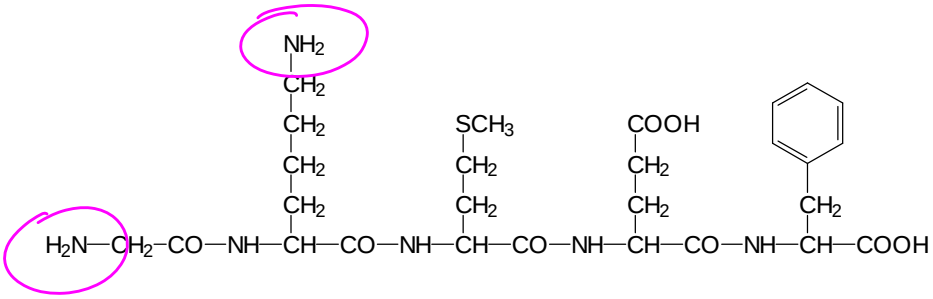
A=E

nitro drawn out

A, B, C are resonance structures

⊖ cannot end up here

10. The peptide shown below will react with how many equivalents of Sanger's Reagent? (work out your answer) 2



11. A peptide with 12 amino acids has the *composition* (not sequence) $AspCys_2Glu_2Leu_2Ser_2Tyr_2Val$. It also has Ser as the N-terminal residue and Cys as C-terminal. Partial acid hydrolysis gave these peptide sequences:

do overlap analysis

SerLeuTyr — SerLeuTyr

TyrCys — LeuTyrGlu

LeuTyrGlu — GluLeuGlu

GluLeuGlu — GluAspTyr

SerValCys — TyrCys

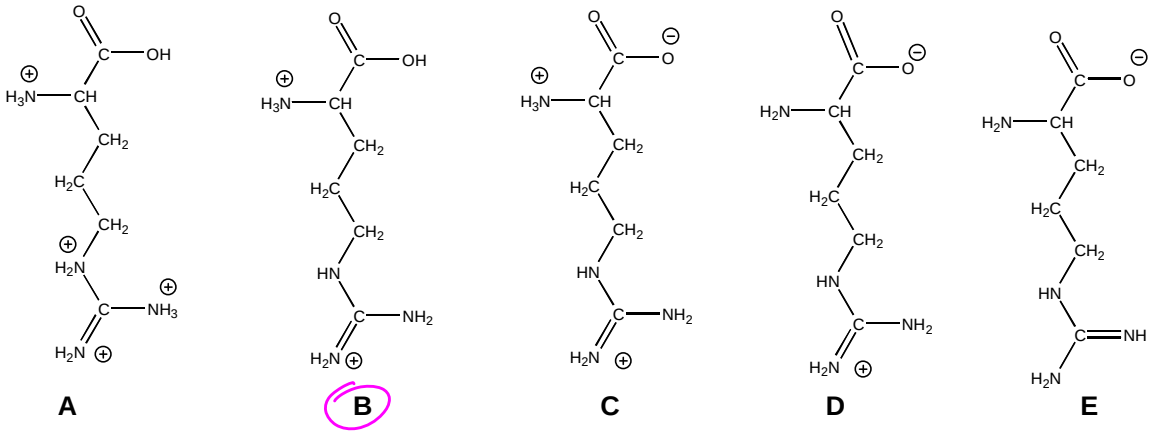
CysSerVal — CysSerVal

GluAspTyr — SerValCys

What is the sequence of the original peptide?

A) SerValCysGluLeuGluAspTyrSerLeuTyrCys
B) SerValCysSerLeuTyrGluLeuGluAspTyrCys
C) SerLeuTyrSerValCysGluLeuGluAspTyrCys
D) SerLeuTyrGluLeuGluAspTyrCysSerValCys
E) SerLeuTyrGluAspTyrGluLeuGluSerValCys

12. Which form of arginine is most likely to exist at pH = 1?



only one guanidinium N is protonated

13. Which one of the following statements best describes how the C-terminal amino acid of an oligopeptide is identified?

A) The oligopeptide is degraded by acid hydrolysis and amino acids are identified by TLC

B) The oligopeptide is treated with carboxypeptidase and, after reaction has occurred, the peptide is analyzed to see which residue has been removed

C) The C-terminal amino acid may be derivatized with Sanger's reagent and identified after oligopeptide hydrolysis by chromatography

D) Carboxypeptidase is used to degrade the peptide, the first amino acid to be released is identified by running amino acid analyses at regular time intervals

E) None of the above

it is not the remaining peptide that is analyzed

14. A pentapeptide was found to have the composition Ala Arg Gly Pro Trp. Reaction of the pentapeptide with Sanger's reagent, followed by hydrolysis, gave the DNP derivative of proline. Treatment of the pentapeptide with carboxypeptidase initially produced alanine. Treatment of the pentapeptide with trypsin gave a tetrapeptide which, when treated with chymotrypsin, produced a tripeptide. Which one of the following is the sequence of the pentapeptide? (note: trypsin cleaves after basic amino acids)

A) Pro Gly Arg Trp Ala

B) Pro Arg Gly Trp Ala

C) Pro Trp Arg Gly Ala

D) Pro Gly Trp Arg Ala

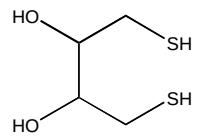
E) Pro Trp Gly Arg Ala

cuts after basic aa

so aa 4 = basic

aa 3 = aromatic

15. Dithiothreitol reacts with disulfide bridges in proteins in the same way as 2-mercaptoethanol or thioacetic acid do. When an excess of dithiothreitol is used, what the are the most likely products of this reaction?

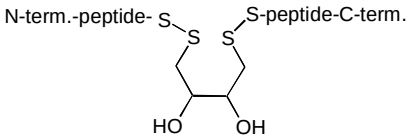


Dithiothreitol

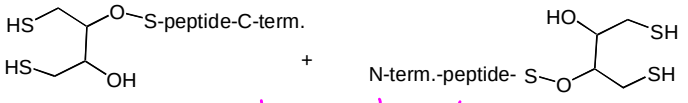
will be reduced

+ N-term.-peptide -S-S-peptide -C-term. → ?

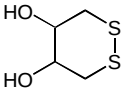
A



B



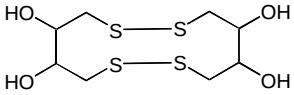
C



intramolecular more likely than inter. (D)

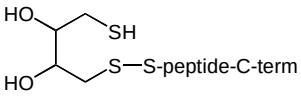
+ N-term.-peptide-SH + HS-peptide-C-term.

D

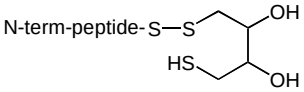


+ N-term.-peptide-SH + HS-peptide-C-term.

E



+



16. Which one of the following hydrogen bonds (shown as dotted bonds) best represents the type of hydrogen bond that keep the α-helix and the β-sheet from falling apart?

A) O-H·····O=C
B) O-H·····NH=C
C) N-H·····NH=C
D) N-H·····O=C between NH and amide C=O
E) N·····H-N=C

17. Oxytocin, a hormone peptide of nine amino acids, is widely used in obstetrics to induce uterine contractions. There is an intramolecular disulfide bond which must be reduced before sequencing.

Reduced oxytocin has the composition Asn Cys_2 Gln Gly Ile Leu Pro Tyr

Partial hydrolysis of reduced oxytocin led to the following fragments

Asn-Cys
Cys-Tyr
Tyr-Ile-Gln
Cys-Pro-Leu
Ile-Gln
Leu-Gly
Gln-Asn-Cys

Reaction of reduced oxytocin with carboxypeptidase showed glycine as the first liberated amino acid.

Which one of the following is the sequence of oxytocin?

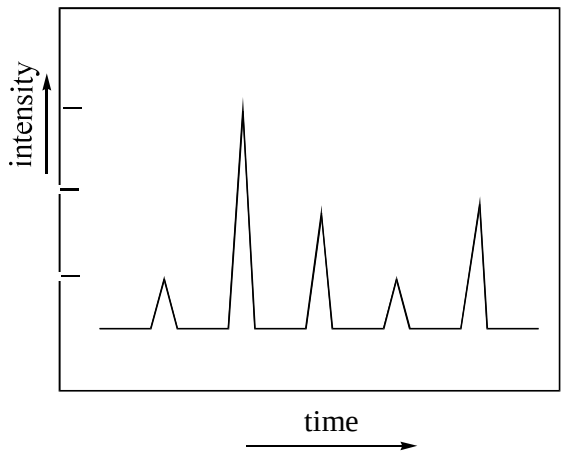
A) Asn Cys Tyr Ile Gln Cys Pro Leu Gly
B) Gln Asn Cys Tyr Ile Cys Pro Leu Gly
C) Cys Pro Gln Asn Cys Tyr Ile Leu Gly
D) Cys Tyr Ile Gln Asn Cys Pro Leu Gly
E) Gln Asn Cys Tyr Ile Cys Pro Leu Gly

- chart shows 5 diff a.a. 1:3:2:1:2
= 8 residues in peptide
note: a) intensity ∝ amount
b) time = identity

AA.8

18. The graphic below represents the recording from an amino acid analyzer, run at pH 5.5 using the column type discussed in the class notes (negatively charged and hydrophobic). Which one of the following polypeptide sequences best fits these data? (Note that the answers are polypeptide sequences, not order of elution of the amino acids!)

⊖ charged first
⊕ charged last



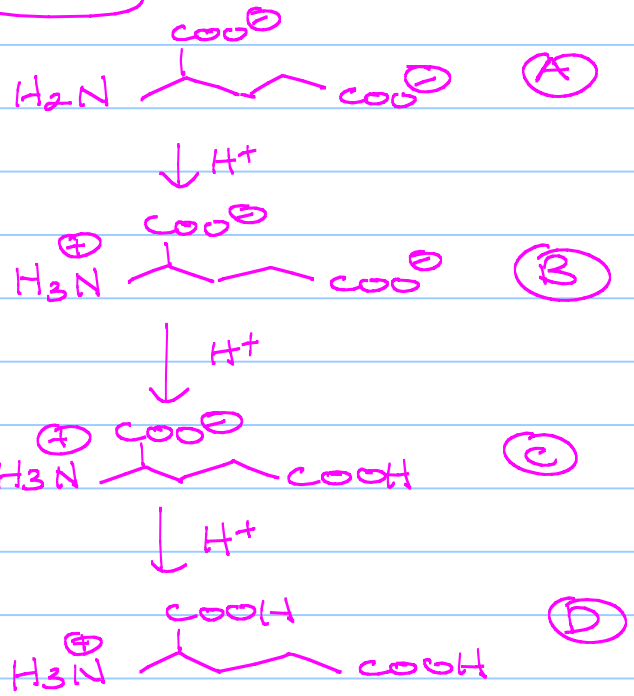
A) Ser Arg Asp Phe Arg His Phe Ser Ser
B) Arg Phe Lys Lys Phe Asp Lys Glu Glu ← 2 Glu should elute early (no peak of int = 2 early on plot)
C) His Arg Ala Glu Asp Arg Arg Ala Asp
D) Ile Val Ala Ile Lys Lys Ala Gly Arg ← no 3 same aa
E) His Arg His Phe Ser Arg Ser Lys Arg. ← 3 Arg should elute late

19. Briefly describe how the elution order would change if the column were positively charged and hydrophobic, instead of being negatively charged and hydrophobic. Assume that the experimental conditions (pH and solvent) are the same.

20. Disodium glutamate was titrated with HCl. Draw the predominant form(s) of the amino acid produced after the addition of 0.0, 0.5, 1.0, 1.5, 2.0, 2.5, and 3.0 equivalents of HCl.

Asp = neg
Ser = polar
Phe = hydrophobic
His = some + charge at pH 5.5
Arg = positive

#20



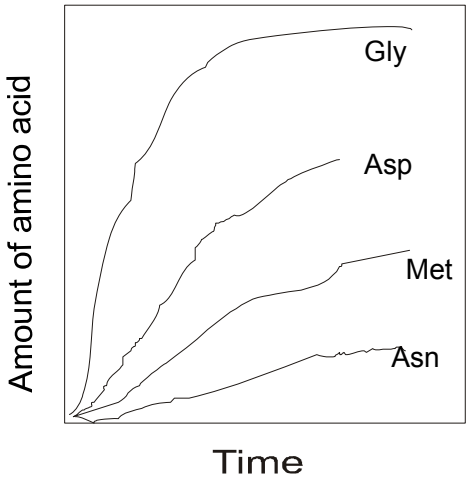
NH_2 = most-basic group

$COO^\ominus$ closest to $NH_3^\oplus$ is most-stable (i.e. least-basic) due to inductive effect

equiv H^+ added to (A)	predominant forms
0	A
0.5	1:1 A:B
1.0	B
1.5	1:1 B:C
2.0	C
2.5	1:1 C:D
3.0	D

21. An oligopeptide was analyzed. Given the data below, what is its sequence?

- AA analysis revealed the composition Asp Asn Glu_2 Gly Lys Met_2 Phe Pro_2
- Carboxypeptidase digestion gave the results shown in this plot



N ~ Asn Met Asp Gly - COOH
∴ only D or E

- Sanger N-terminal analysis afforded the DNP derivative of glutamic acid

N - term

- Treatment of the peptide with cyanogen bromide gave three fragments. Sanger N-terminal analysis of these three fragments gave the DNP derivatives of Glu, Pro, and Asp.

cleaves after Met
(did not examine in class)

- Cleavage of the oligopeptide with trypsin gave two fragments. Sanger analysis of these two fragments both gave the DNP derivative of Glu

cleaves after basic aa
∴ D

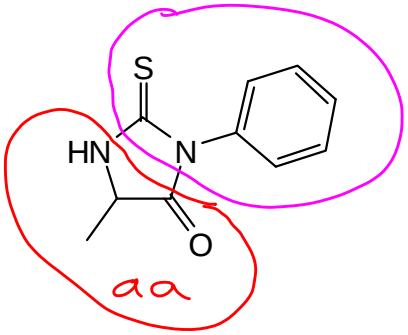
- Cleavage of the oligopeptide with chymotrypsin gave two fragments. Sanger analysis of these two fragments gave DNP derivatives of Glu and Lys.

cleaves after hydrophobic
∴ D

A) Glu Pro Met Pro Gly Lys Phe Met Asp Asn Glu
B) Glu Met Pro Pro Phe Lys Gly Asp Met Asn Glu
C) Gly Asp Met Asn Glu Pro Pro Met Phe Lys Glu
D) Glu Met Pro Pro Phe Lys Glu Asn Met Asp Gly
E) Glu Pro Met Pro Lys Phe Glu Asn Met Asp Gly

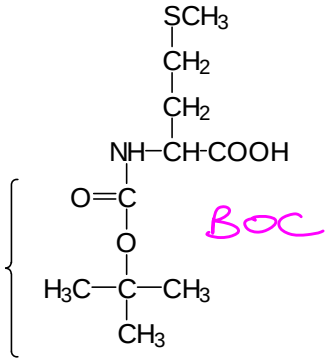
Ph-N=C=S from PITC

22. The compound shown on the right is the phenylthiohydantoin derivative of which amino acid?



A) Alanine
B) Phenylalanine
C) Cysteine
D) Proline
E) Cannot tell, because every amino acid forms the same compound

23. Which statement about the group marked by { in the structure shown is most correct?

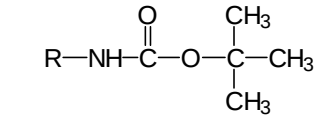


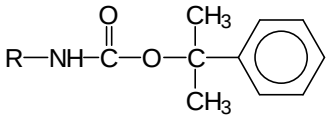
A) It makes the amino acid coloured and easier to detect
B) It acts as an activating group, making peptide bond formation easier
C) It acts as a protecting group, keeping the NH_2 of the amino acid from reacting as a nucleophile
D) It acts to protect the amino acid against destruction in acid
E) It provides a thermodynamic driving force for peptide bond formation, by releasing CO_2

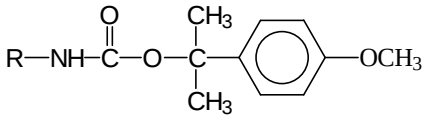
24. In Merrifield's method for protein synthesis, the polymer is used…

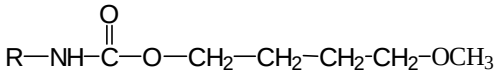
A) To keep the growing peptide soluble
B) To provide a suitable "solvent" for the reactions
C) To prevent undesired side reactions by limiting access by reagents to the peptide chain
D) To make the growing peptide insoluble but accessible
E) To provide essential catalytic groups

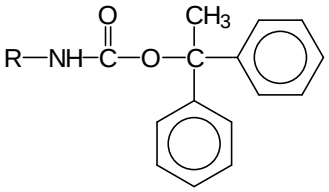
25. Which one of the following compounds will NOT cleave on mild treatment with CF_3COOH?

a) 

b) 

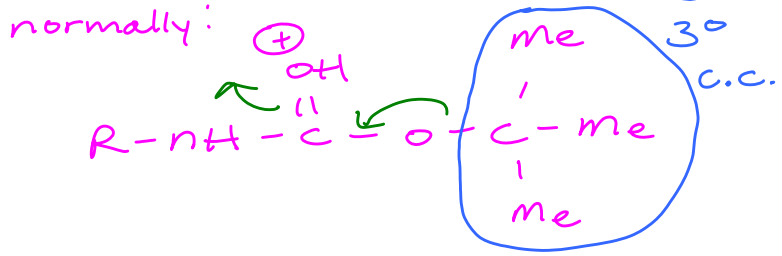
c) 

d) 

e) 

deprotection is by E1, so need a stable carbocation

normally:



26. Which statement about the Merrifield synthesis of proteins is incorrect?

A) The method relies on synthesizing the polypeptide as an insoluble polymer bound chain, which can be separated from any solvents or reactants by filtration

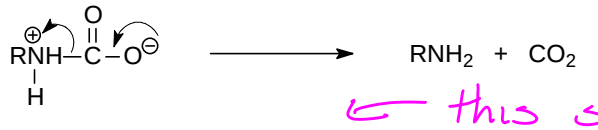
B) The method is conveniently automated, with bottles of all 20 protected amino acids and the various solvents and reagents connected to a reaction vessel through computer controlled valves

C) Adding another residue involves the use of DCC to form an amide bond between the terminal COOH of the growing chain and an amino acid with the COOH protected. C-term attached to polymer

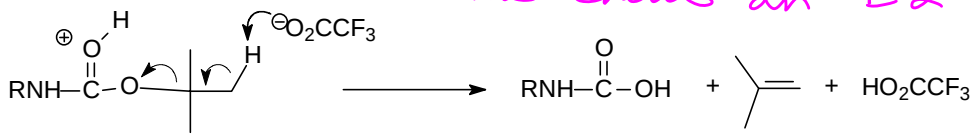
D) It is possible to use excess amounts of reagents to push reactions to completion, because the excess can be removed by filtration.

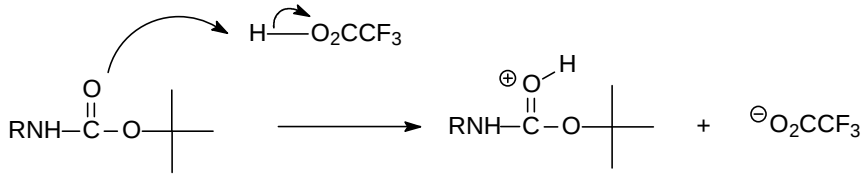
E) The final product peptide can be removed from the polymer by treating with strong acid, typically HBr.

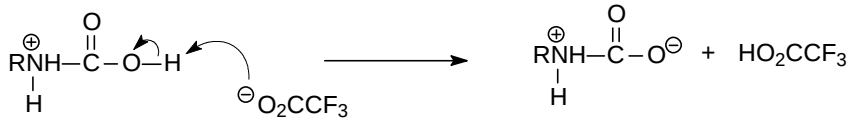
27. Which one of the following is least likely to be a step in the deprotection of a BOC-protected amino acid?

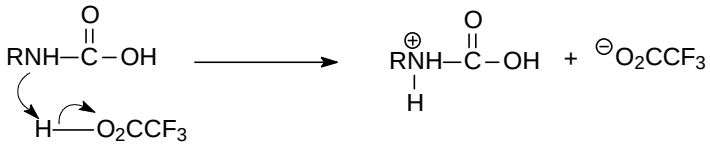
A 

this shows an E2 reaction

B 

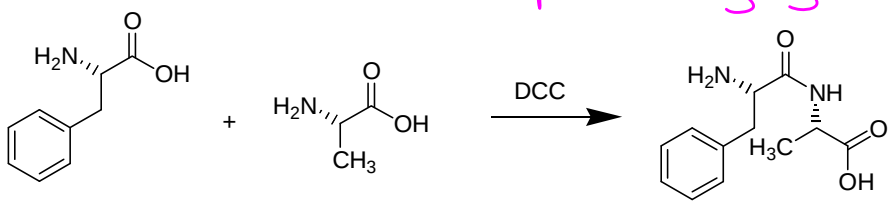
C 

D 

E 

28. Which one of the following statements best explains why the reaction shown below would not give a satisfactory yield?

needs protecting groups



A) DCC causes racemization of amino acids

B) There is nothing to stop each reactant from undergoing self-condensation

C) There is no leaving group on the reacting carbonyl group

D) An amino group is not nucleophilic enough without a protecting group on it

E) A carboxylic acid group is not electrophilic enough without a protecting group.

29. Write out a detailed, arrow-pushing mechanism for the DCC-mediated coupling of acetic acid and ethylamine. see notes

30. Which one of the following pairs of ions would be most strongly attracted to each other in aqueous solution?

A) Na^{+} PO_4^{3-}
B) Ca^{2+} SO_4^{2-}
C) Fe^{3+} Cl^{-}
D) Zn^{2+} ClO_4^{-}
E) Al^{3+} PO_4^{3-} largest charges

31. There is a bacterial protein which binds sulfate ion (SO_4^{2-}) as part of the process of transporting sulfate. Which one of the following ions is least likely to act as an inhibitor of this binding? inhibitor should resemble substrate

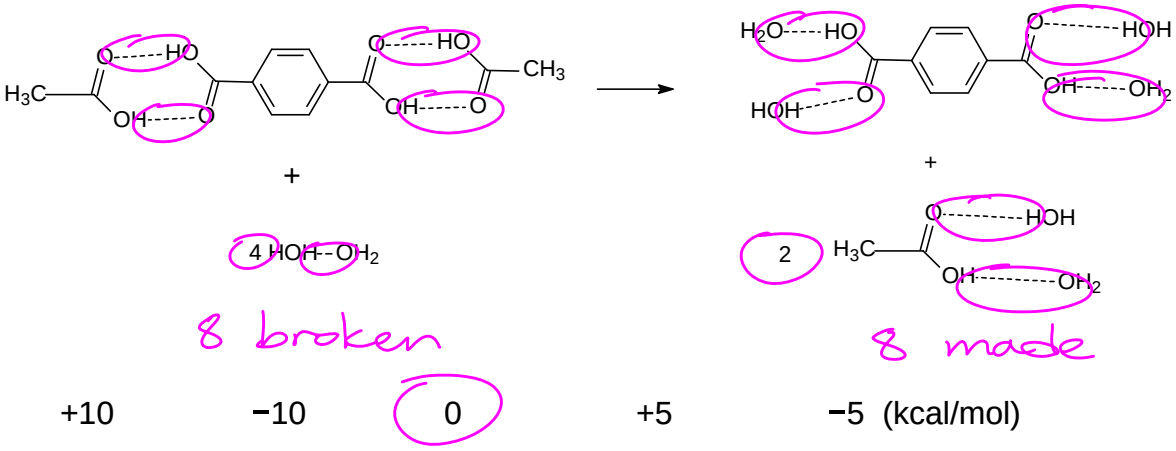
HPO_4^{2-} SeO_4^{2-} $CH_3PO_3^{2-}$ MnO_4^{2-} $CH_3SO_3^{-}$ 1-

32. Which one of these statements about enzyme-substrate binding is correct?

A) If a hydrogen bond can form between enzyme and substrate it is likely to make the overall binding energy more favorable by 5 kcal/mole
B) In the absence of substrate, hydrogen bond forming groups in the active site will be missing this stabilizing interaction
C) Hydrogen bonding mainly contributes to the strength of binding, but generally does not control orientation
D) Hydrogen bonding is insensitive to the acidity of the OH or NH bond involved in it
E) Formation of a single hydrogen bond is unlikely to have much effect on binding energy but can have a strong effect on orientation and specificity

H-bond formed between ES displaces water

33. Given the average strength of a hydrogen bond is 5 kcal/mol, what is the overall free energy change (ΔG) of the following reaction?



34. Biological molecules often have phosphate or pyrophosphate monoester groups. Which one of the following statements regarding this is least correct?

A) The phosphate or pyrophosphate provides a handle for electrostatic binding of the molecule by an enzyme

B) Phosphates or pyrophosphates will accept hydrogen bonds, helping give specific binding to enzymes

C) In the presence of an enzyme, phosphate and pyrophosphate are good leaving groups at physiological pH

D) The introduction of phosphates or pyrophosphates does not require energy — needs ATP

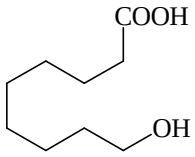
E) Phosphates or pyrophosphates are hydrophilic and can make organic molecules water soluble

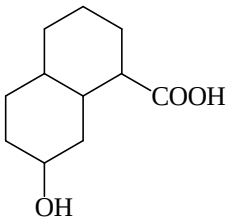
35. What types of interactions are likely involved in the *initial* binding of a substrate to an enzyme? Circle all that apply.

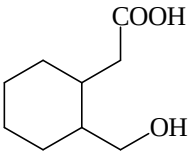
- Hydrophobic interactions
- Hydrogen bonding
- Covalent bonding ← during reaction
- Electrostatic interactions

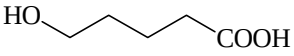
36. Which one of the following compounds would you expect to undergo the most rapid acid catalyzed lactonization?

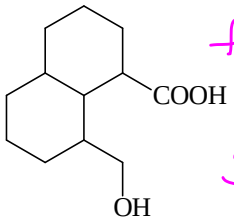
groups too far away

A 

B 

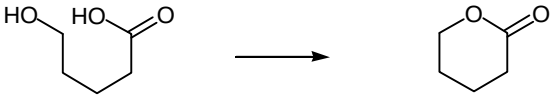
C 

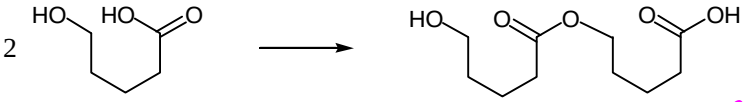
D 

E 

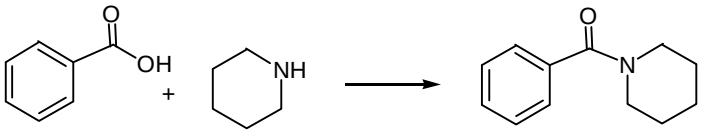
fewest degrees of freedom and groups are close enough

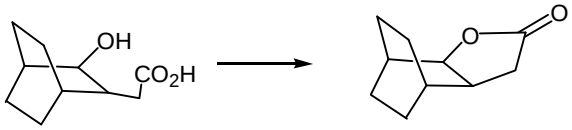
37. Which one of the following reactions gives a poor yield of the product shown when a condensation reagent, such as DCC, is added to the reactant(s)??

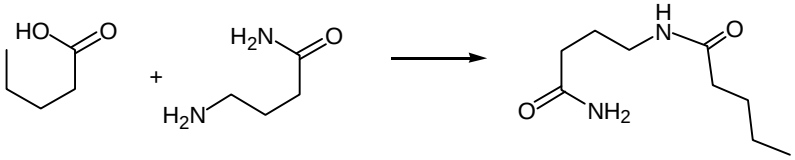
A 

B 

intramolecular (A) more favourable

C 

D 

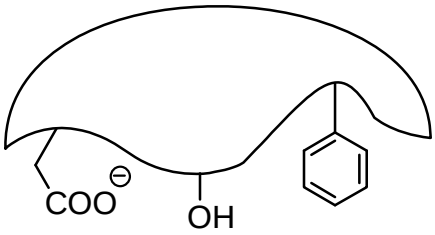
E 

(C + E have no choice but to react intermolecularly)

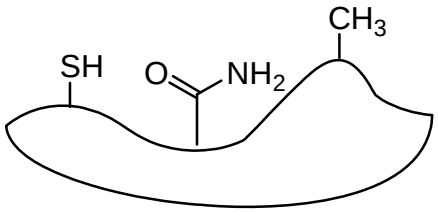
38. The active site of an enzyme is shown on the right. The binding of which of substrates A – E would result in the most positive ΔG of reaction?

$E + S \rightleftharpoons ES$

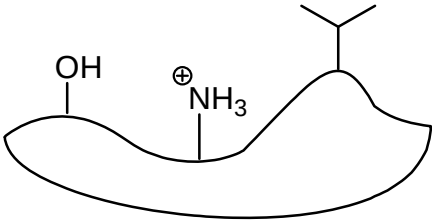
least favourable



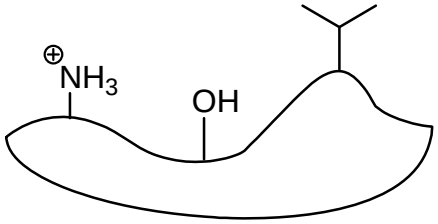
A)



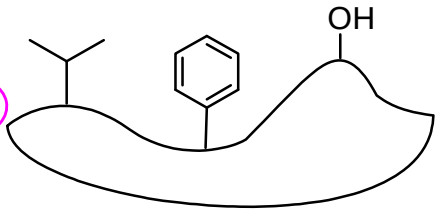
B)



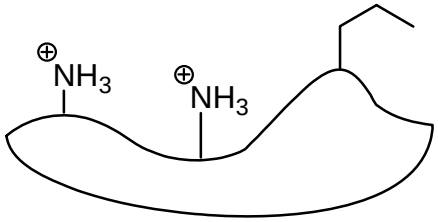
C)



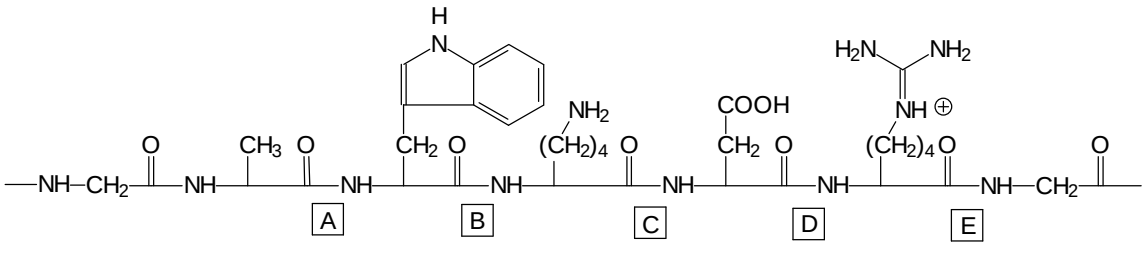
D)



E)

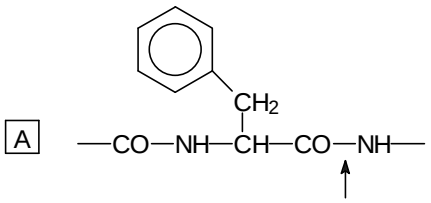


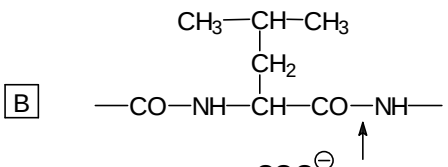
39. Which one of the peptide bonds in the molecule shown would be hydrolyzed the fastest with chymotrypsin?

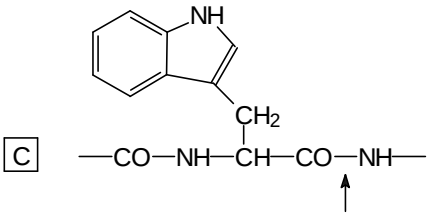


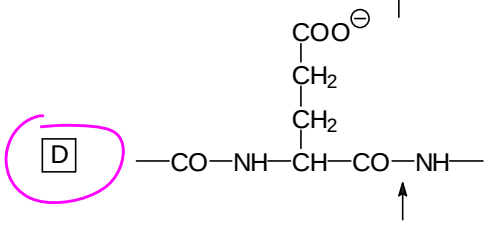
after aromatic when N → C

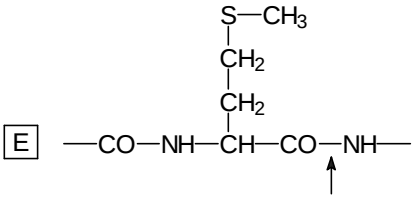
40. Which one of the following amino acid residues is least likely to be cleaved by chymotrypsin at the bond shown?





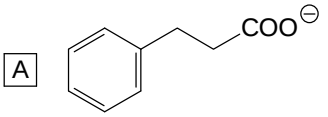


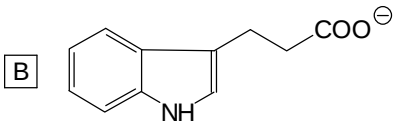


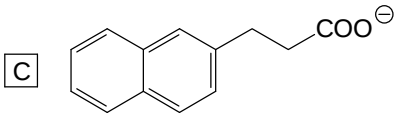


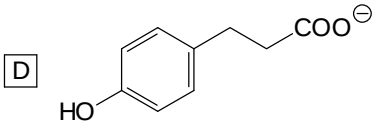
⊖ charge would not bind to hydrophobic pocket

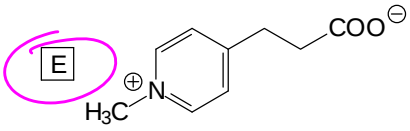
42. Which one of the following compounds would not be expected to be an inhibitor towards chymotrypsin?





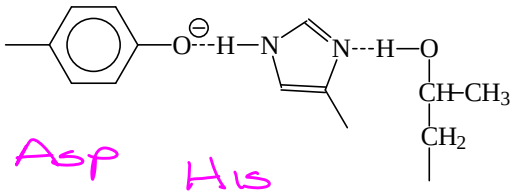


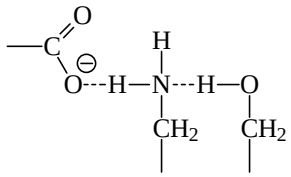




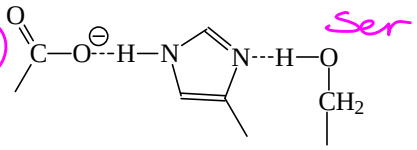
same reason as previous

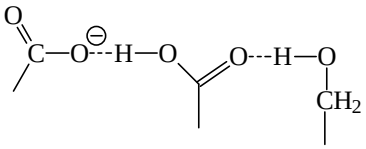
43. Which one of the following arrays of functional groups is known as the catalytic triad in chymotrypsin?

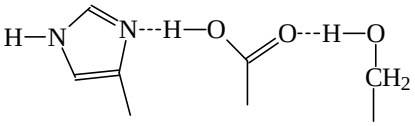
A 

B 

Asp His Ser

C 

D 

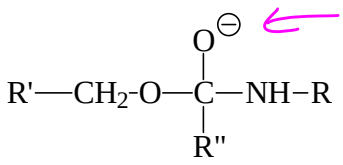
E 

44. Chymotrypsin catalyzes the hydrolysis of peptides. During the mechanism of action of chymotrypsin there is an intermediate with one fragment of the original peptide covalently bound to the enzyme while the other fragment drifts away. This intermediate is best described as…

A) An anhydride
B) An ester acyl enzyme
C) An amide
D) A thioester
E) A tetrahedral intermediate

implies Ser has attacked, tetrahedral intermediate collapsed, and fragment displaced

45. In the mechanism of action of chymotrypsin, a tetrahedral intermediate has been proposed. Describe how is this intermediate made more stable by the enzyme.

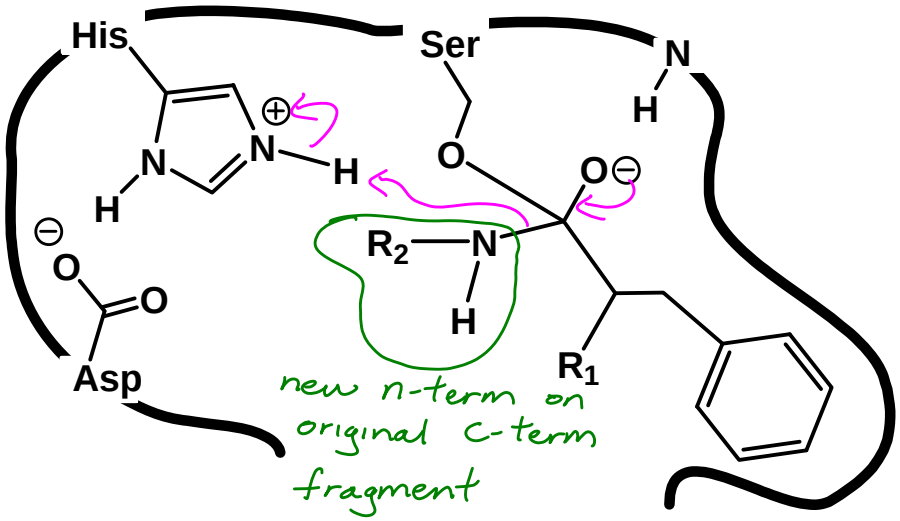


← H-bonding to amide backbone

46. Which of the following statements about the *first* tetrahedral intermediate in the chymotrypsin catalyzed hydrolysis of a peptide bond is/are correct? (Circle)

- When this intermediate collapses, the charge relay system relays the negative charge (of the tetrahedral intermediate) from the oxyanion hole to a carboxylate group.
- Hydrogen bonding from the imidazole group of the charge relay system assists the amino group to leave when the tetrahedral intermediate collapses.
- This is an intermediate on the way from an amide to an ester
- This intermediate is stabilized by hydrogen bonding in the oxyanion hole
- Thisintermediate is held in place both by hydrogen bonding and also by hydrophobic binding of the aromatic side chain to the hydrophobic pocket
- Without the enzyme, the formation of this intermediate would be unfavourable

47. Which one of A – E does NOT correctly describe the current state of the chymotrypsin-substrate complex below and the next mechanistic step that occurs? (You may wish to add hydrogen bonds and the mechanistic arrows).



A) This intermediate is part of a nucleophilic acyl substitution reaction.

B) The aromatic ring interacts with the enzyme via hydrophobic interactions.

C) In the next step, His protonates the leaving group.

D) The current tetrahedral intermediate is stabilized by hydrogen bonding to the enzyme backbone.

E) In the next step, the N-terminal fragment of the original substrate departs.