Isoelectric Point (pI)

Peptide Synthesis

4/21/2023

A Brief Reminder about pH and pKa

$$pH = -\log[H^+]$$

describes H^+ content in a solution

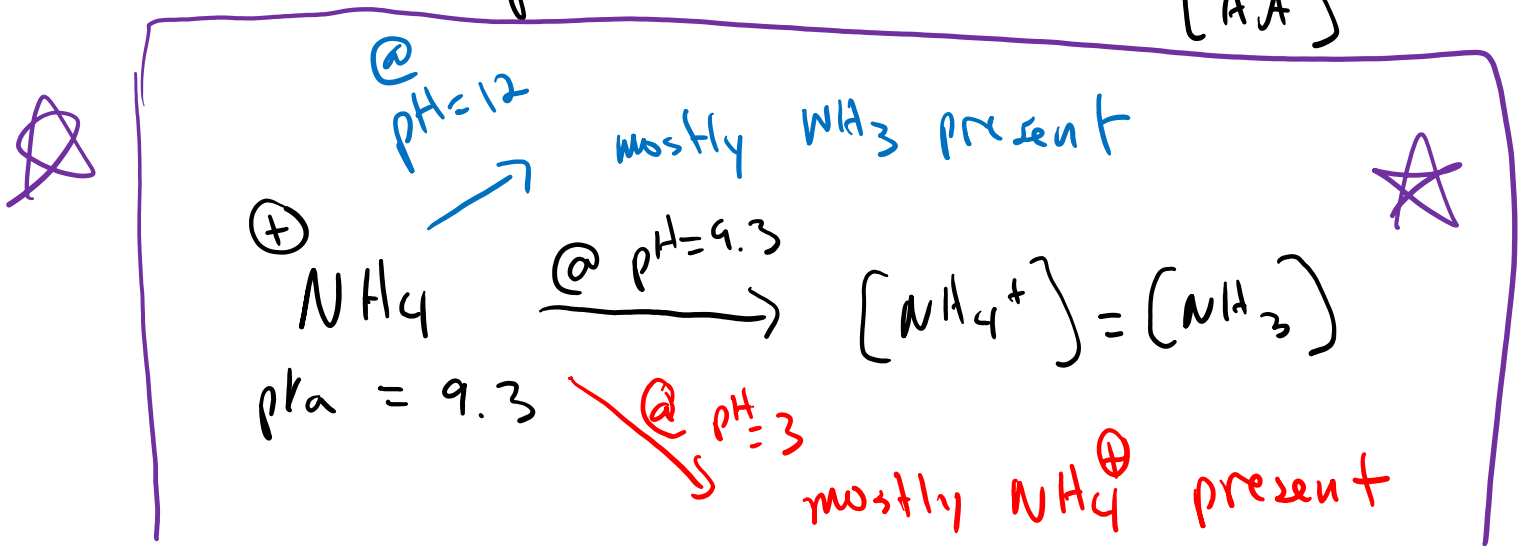
$$HA \rightleftharpoons H^+_{(aq)} + A^-$$

$$Ka = \frac{[H^+][A^-]}{[HA]}$$

$$pKa = -\log Ka$$

describes acidity of a molecule or part of a molecule

$$pH = pKa + \log\frac{[A^-]}{[HA]}$$



if $[A^-] = [HA]$

then pH = pKa

pH above pKa - more A^-

below more HA

Amino Acid pKa Table

provided on exams

TABLE 25.2 THE pK_a VALUES FOR TWENTY NATURALLY OCCURRING AMINO ACIDS

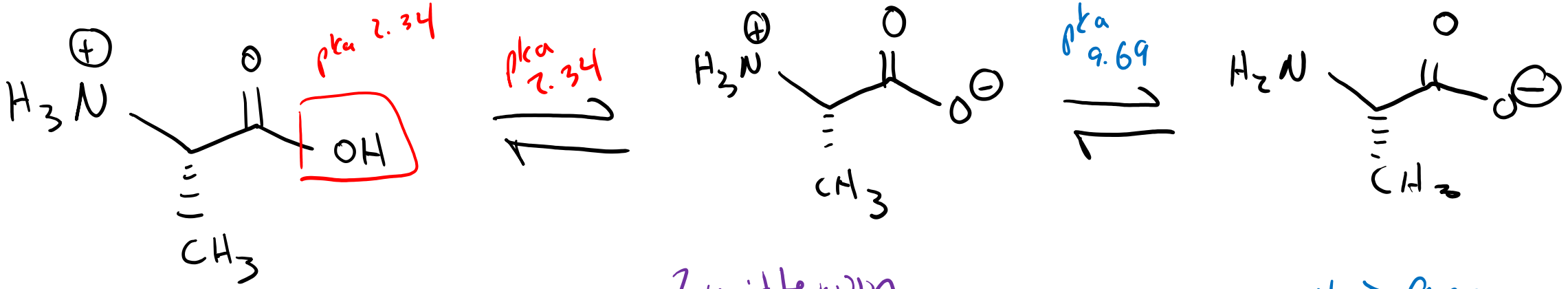
AMINO ACID	α-COOH	α-NH_3^+	SIDE CHAIN
Alanine	2.34	9.69	—
Arginine	2.17	9.04	12.48
Asparagine	2.02	8.80	—
Aspartic acid	1.88	9.60	3.65
Cysteine	1.96	10.28	8.18
Glutamic acid	2.19	9.67	4.25
Glutamine	2.17	9.13	—
Glycine	2.34	9.60	—
Histidine	1.82	9.17	6.00
Isoleucine	2.36	9.60	—
Leucine	2.36	9.60	—
Lysine	2.18	8.95	10.53
Methionine	2.28	9.21	—
Phenylalanine	1.83	9.13	—
Proline	1.99	10.60	—
Serine	2.21	9.15	—
Threonine	2.09	9.10	—
Tryptophan	2.83	9.39	—
Tyrosine	2.20	9.11	10.07
Valine	2.32	9.62	—

Isoelectric Point

pH where Zwitterion is most prevalent (neutral form)

pI → not -log I

Alanine



pH < 2.34

Zwitterion

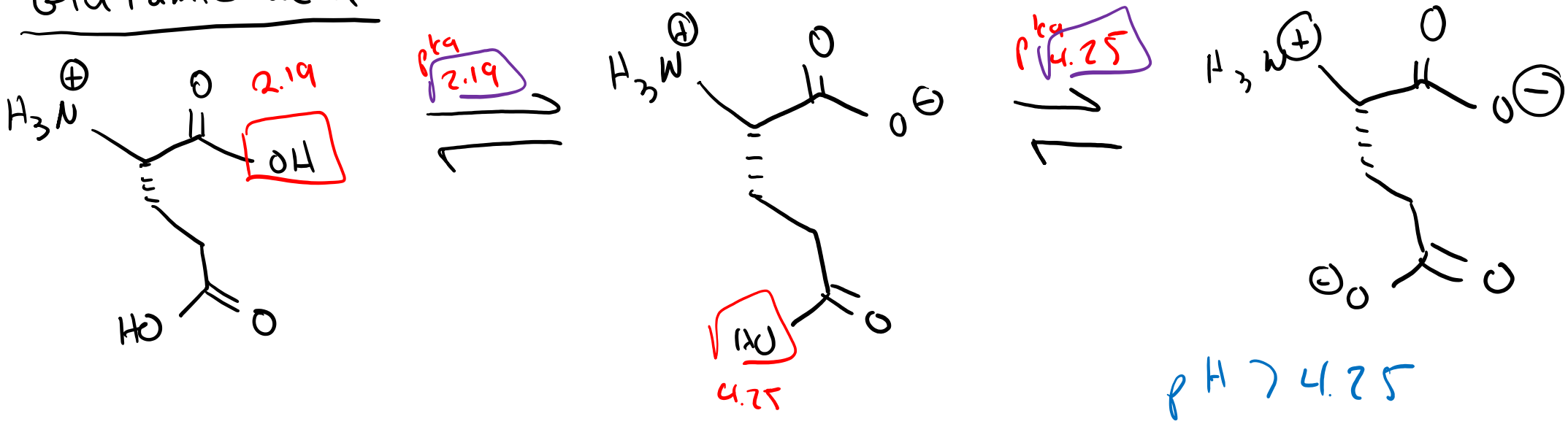
pH > 9.69

$$pI = \frac{2.34 + 9.69}{2}$$

pI = 6.02 max conc. of Zwitterion when pH = 6.02

Isoelectric Point

Glutamic acid



pH < 2.19

Zwitterion

pH > 4.25

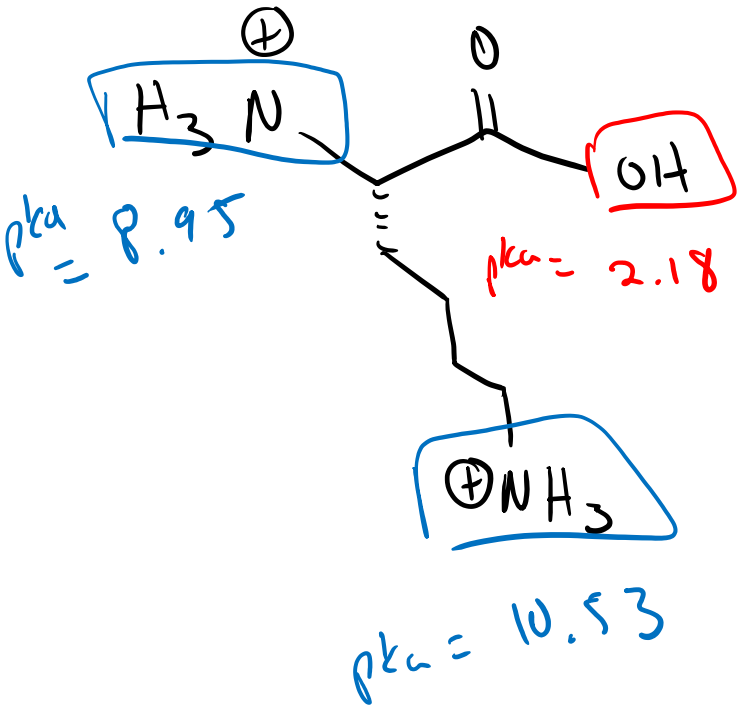
$$pI = \frac{2.19 + 4.25}{2} = 3.22$

Isoelectric Point

Shortcut when 3 pka's involved

pI = avg of two most similar pka's

Lysine



$$pI = \frac{8.95 + 10.53}{2}$$

$$= 9.74$$

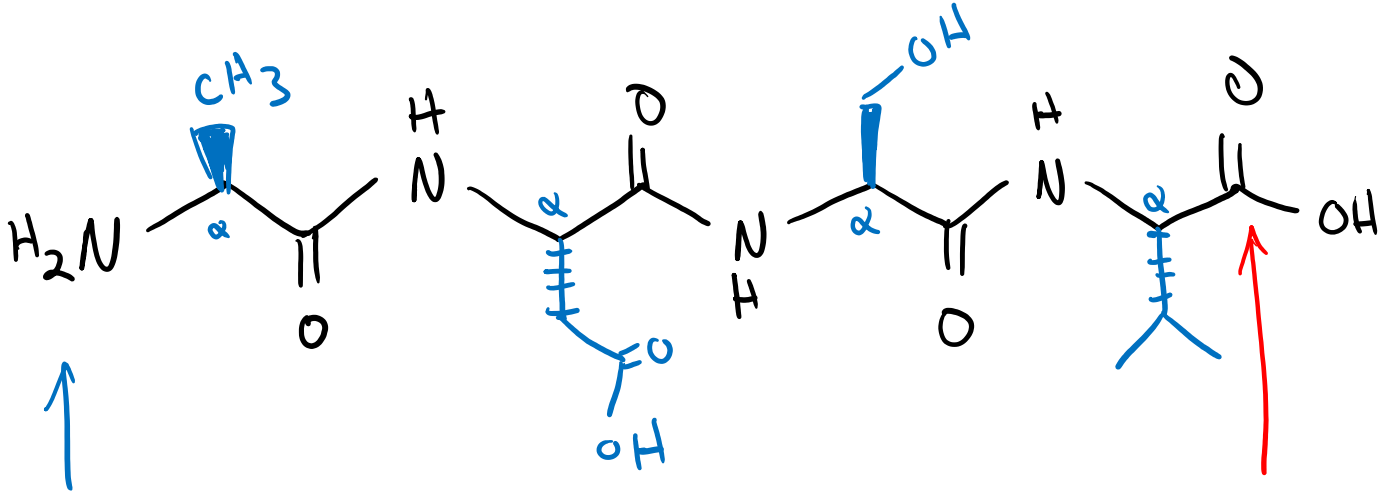
Drawing Peptide Chains

chain of several amino acids

(25.4)

Draw Ala - Asp - Ser - Val

tetrapeptide



N-terminus

amine end of chain

C-terminus

carboxylic acid end of chain

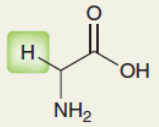
① Draw N-terminus on left side (N, α, C's)

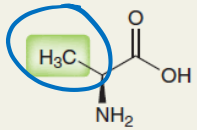
② Add R groups to α carbons (using chart)

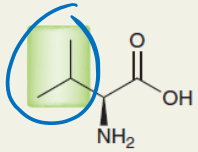
③ Add stereochem (L-amino acids only)

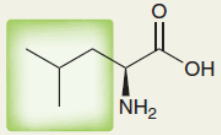
R group "up" - wedge

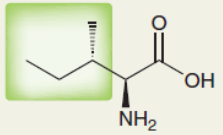
R group "down" - dash

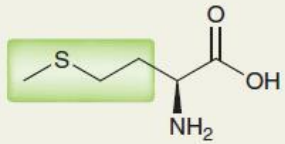
Glycine  Gly G

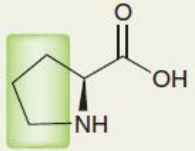
Alanine  Ala A

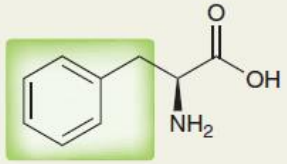
Valine  Val V

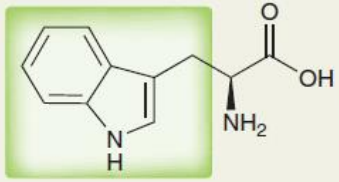
Leucine  Leu L

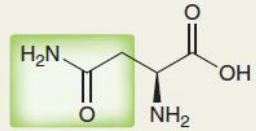
Isoleucine  Ile I

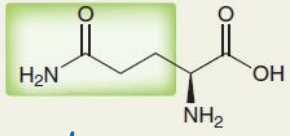
Methionine  Met M

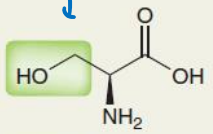
Proline  Pro P

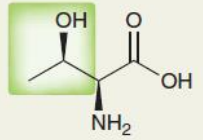
Phenylalanine  Phe F

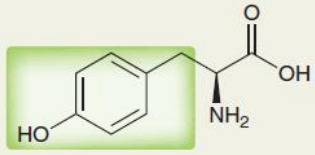
Tryptophan  Trp W

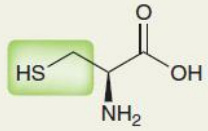
Asparagine  Asn N

Glutamine  Gln Q

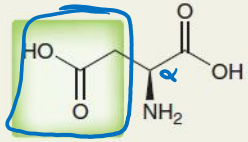
Serine  Ser S

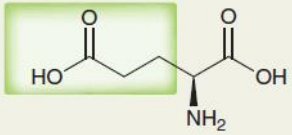
Threonine  Thr T

Tyrosine  Tyr Y

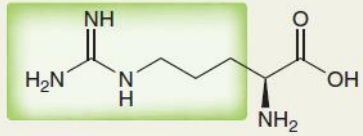
Cysteine  Cys C

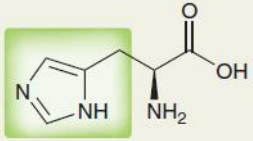
Amino acids with acidic side chains

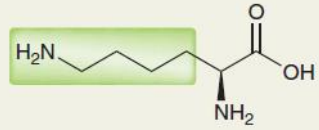
Aspartic acid  Asp D

Glutamic acid  Glu E

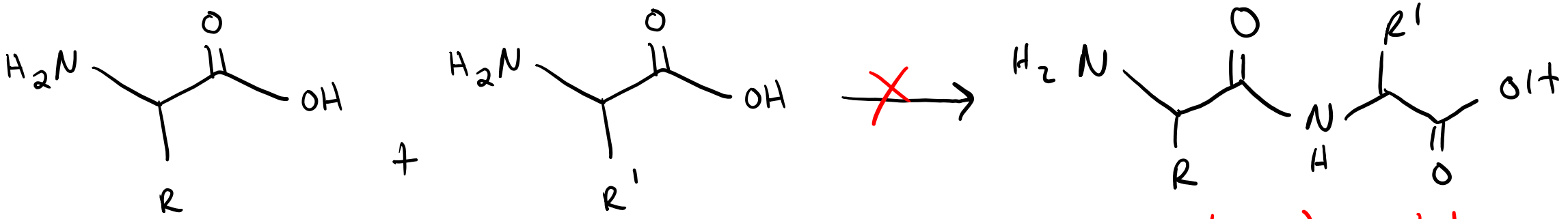
Amino acids with basic side chains

Arginine  Arg R

Histidine  His H

Lysine  Lys K

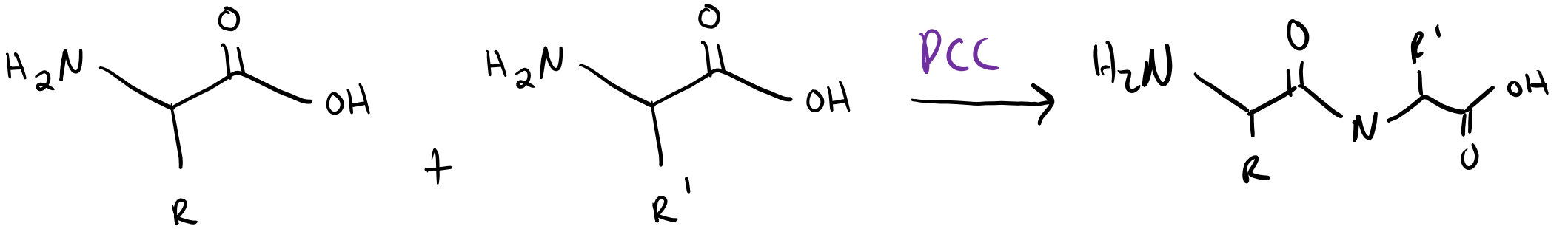
Synthesis of Peptides: Linking Amino Acids Together (25.6)



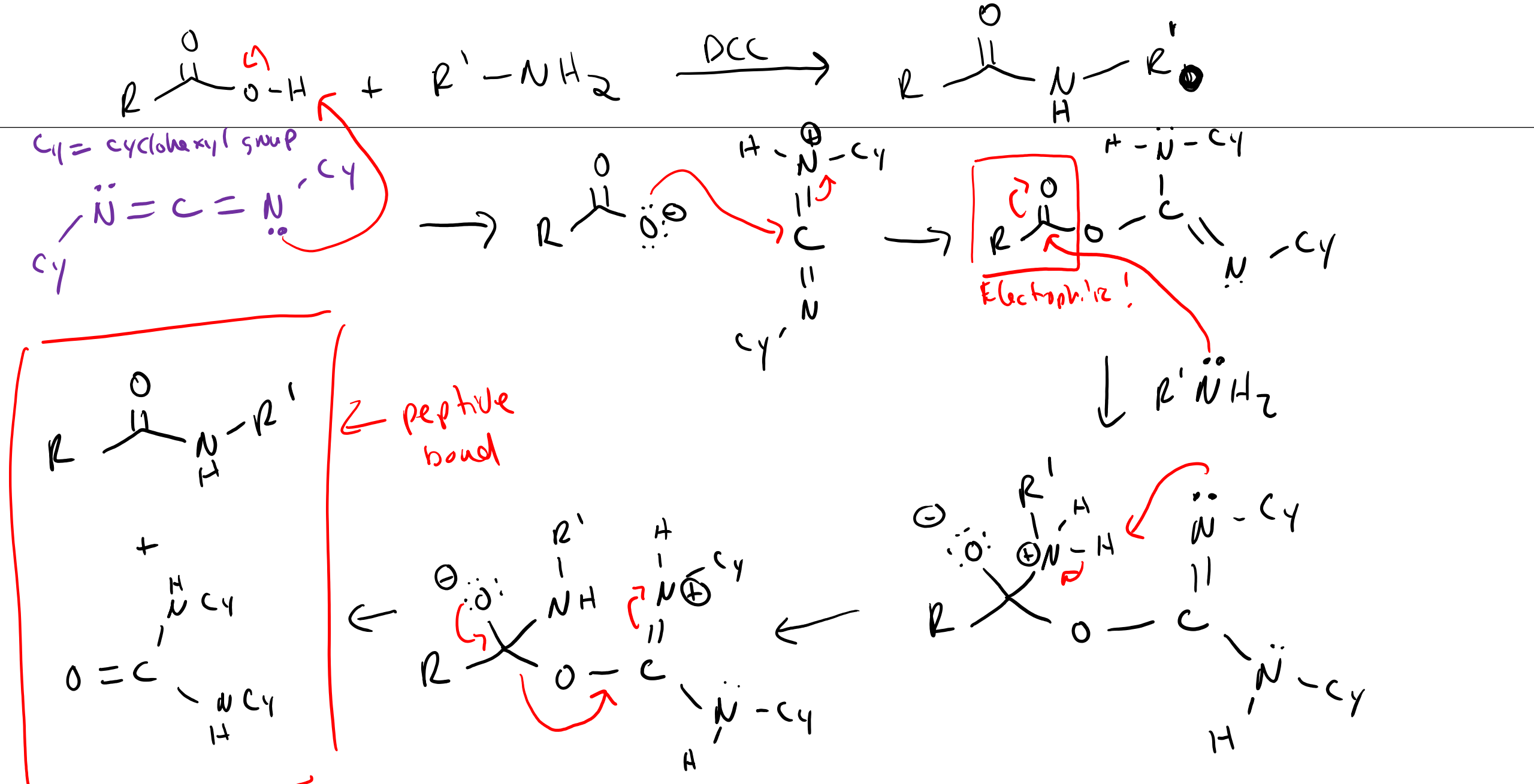
carboxylic acid + amine doesn't directly form an amide!

desired peptide

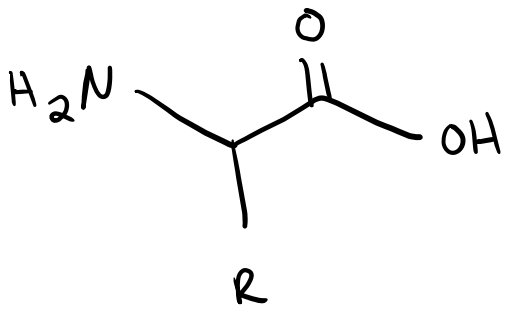
Solution use DCC to promote rxn.

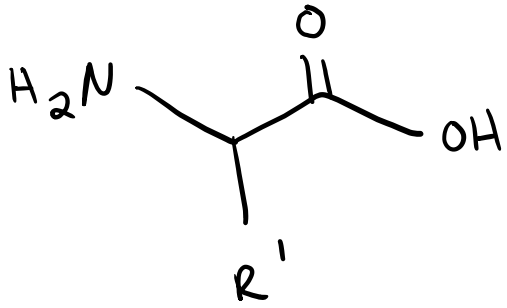


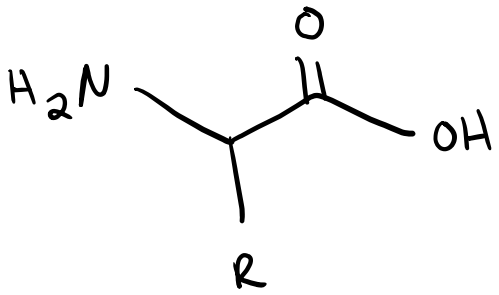
Peptide Bond Formation with DCC: Mechanism

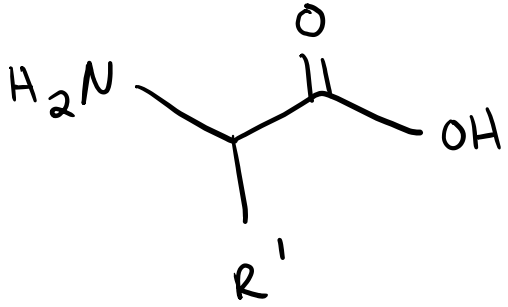


Peptide Synthesis: Protecting Groups









Protecting the Amine Group with “Boc”