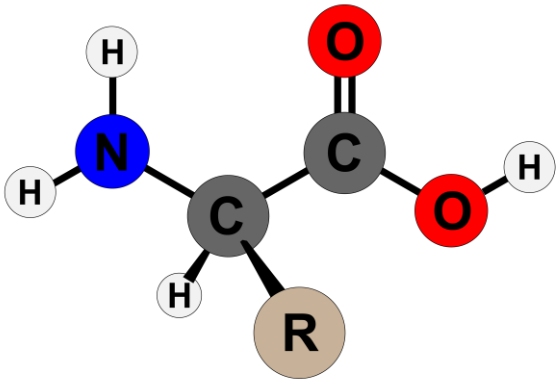
Protein-1



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Recommended Textbook:

Chapter 24 in *Organic Chemistry*, 8^{th} Edition, L. G. Wade, Jr., **2010**, Prentice Hall (Pearson Education)

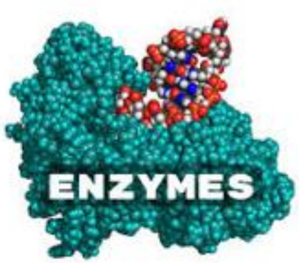
Key concepts:

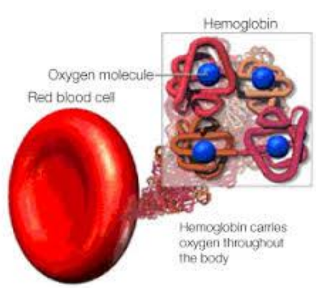
- What is Protein?
- What is amino acid

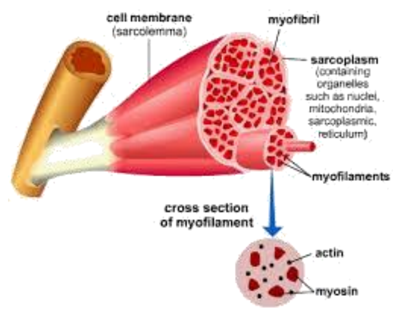
Protein

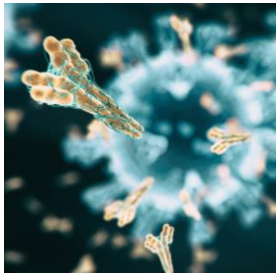
Proteins are the **most abundant** organic molecules in **animals**, playing important roles in all aspects of cell structure and function

Class of Protein	Example	Function of Example
structural proteins	collagen, keratin	strengthen tendons, skin, hair, nails
enzymes	DNA polymerase	replicates and repairs DNA
transport proteins	hemoglobin	transports O_2 to the cells
contractile proteins	actin, myosin	cause contraction of muscles
protective proteins	antibodies	complex with foreign proteins
hormones	insulin	regulates glucose metabolism
toxins	snake venoms	incapacitate prey



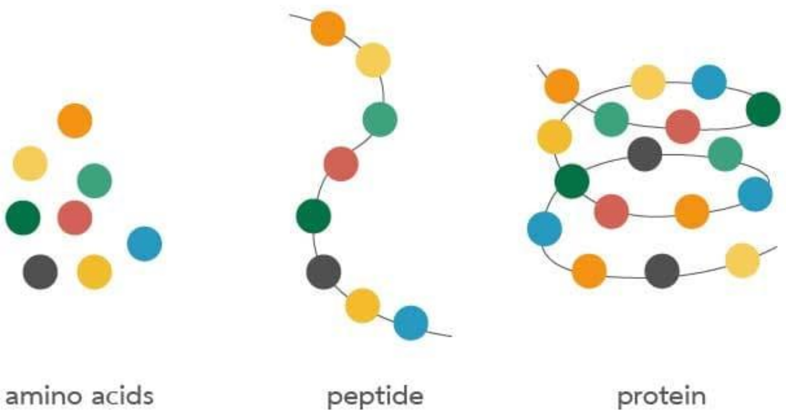






Protein – General structure

- Proteins are **biopolymers** of ***α*-amino acids**, so named because the amino group is bonded to the *α* carbon atom, next to the carbonyl group



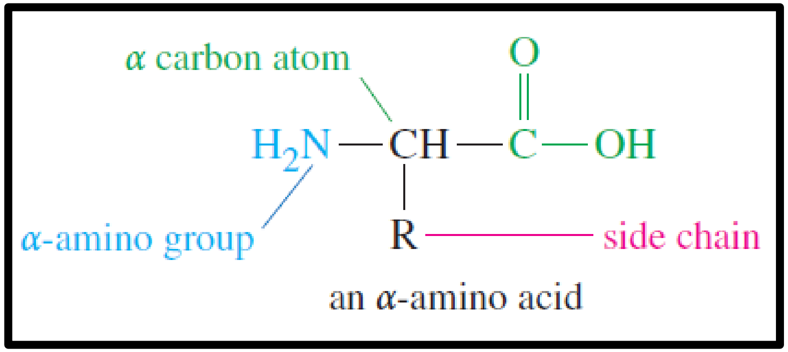
- The amino acid subunits are joined by **amide linkages** called **peptide bonds**

Key concepts:

- What’s the difference between each type of amino acids

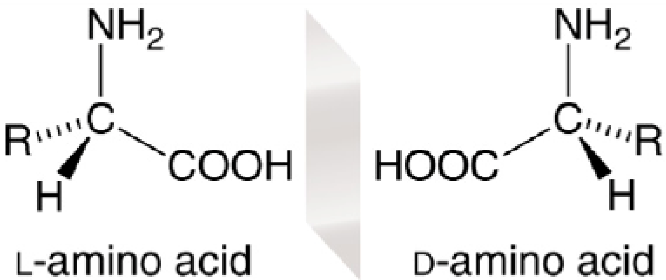
α-Amino Acids

- The simplest *α*-amino acid is **aminoacetic acid**, called **glycine**. Other common amino acids have **side chains** (symbolised by **R**) substituted on the ***α* carbon;** for example, **alanine** is the amino acid with a **methyl side chain**



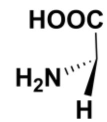
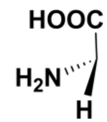
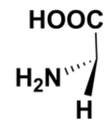
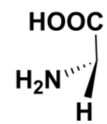
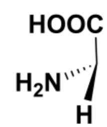
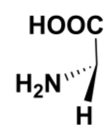
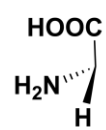
- Except for glycine, the *α*-amino acids are all **chiral** and the chirality centre is at the asymmetric *α* carbon atom

- Nearly all the naturally occurring amino acids are found to have the **(*S*) configuration**

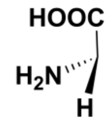
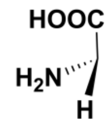
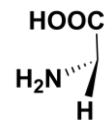
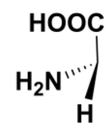
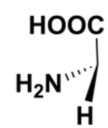
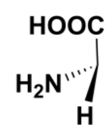
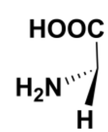


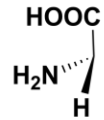
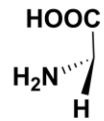
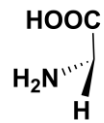
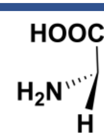
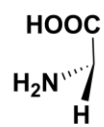
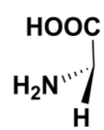
Standard α-Amino Acids

20 **standard** amino acids, grouped according to the chemical properties of side chains

Name	Symbol	Abbreviation	Structure	Functional Group in Side Chain	Isoelectric Point
side chain is nonpolar, H or alkyl					
glycine	G	Gly		none	6.0
alanine	A	Ala		alkyl group	6.0
*valine	V	Val		alkyl group	6.0
*leucine	L	Leu		alkyl group	6.0
*isoleucine	I	Ile		alkyl group	6.0
*phenylalanine	F	Phe		aromatic group	5.5
proline	P	Pro		rigid cyclic structure	6.3

*essential amino acid

Name	Symbol	Abbreviation	Structure	Functional Group in Side Chain	Isoelectric Point
side chain contains an —OH					
serine	S	Ser		hydroxyl group	5.7
*threonine	T	Thr		hydroxyl group	5.6
tyrosine	Y	Tyr		phenolic—OH group	5.7
side chain contains sulfur					
cysteine	C	Cys		thiol	5.0
*methionine	M	Met		sulfide	5.7
side chain is acidic					
aspartic acid	D	Asp		carboxylic acid	2.8
glutamic acid	E	Glu		carboxylic acid	3.2

Name	Symbol	Abbreviation	Structure	Functional Group in Side Chain	Isoelectric Point
side chain is basic					
*lysine	K	Lys		amino group	9.7
*arginine	R	Arg		guanidino group	10.8
*histidine	H	His		imidazole ring	7.6
side chain contains nonbasic nitrogen					
asparagine	N	Asn		amide	5.4
glutamine	Q	Gln		amide	5.7
*tryptophan	W	Trp		indole	5.9

Key concepts:

- What are the acid-base properties of amino acids
- What is “Isoelectric point”, how does it relate to “Electrophoresis”

α-Amino Acids – Acid-Base Properties

- Although we commonly write amino acids with an intact carboxyl –COOH group and amino –NH_2 group, their actual structure is **ionic** and **depends on the pH**

- This structure is called a **zwitterion,** giving them some **unusual properties**

1) More **soluble in water** than they are in common organic solvents

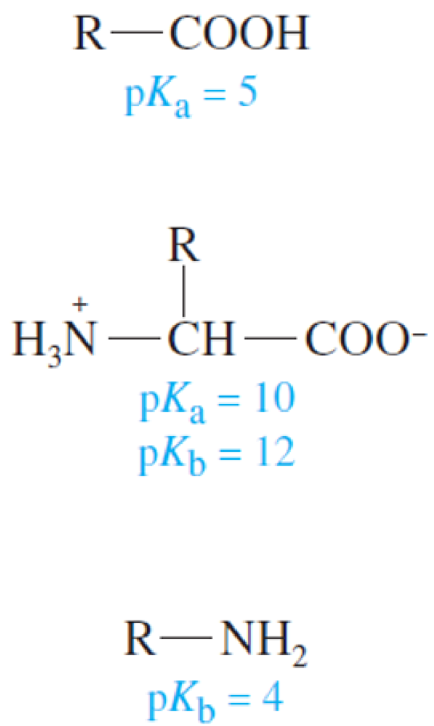
2) High melting points, generally over 200 °C

3) Much **larger dipole moments** than simple amines or simple acids

α-Amino Acids – Acid-Base Properties

- This structure is called a **zwitterion,** giving them some **unusual properties**

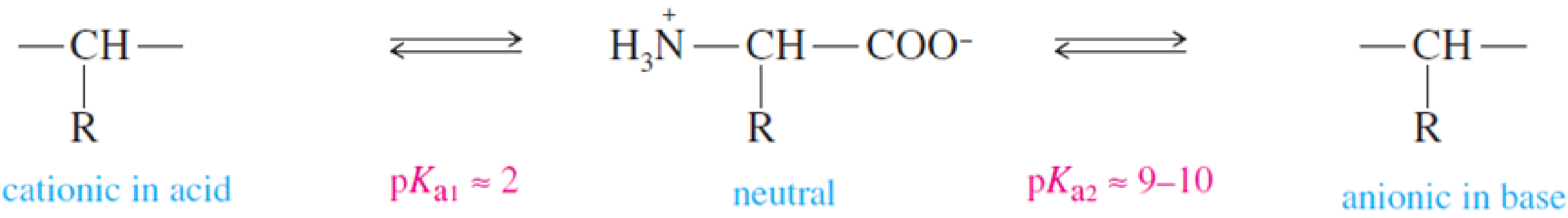
4) Less acidic than most carboxylic acids and **less basic than most amines**



- Because amino acids contain both acidic ($–NH_3^+$) and basic groups ($–CO_2^-$), they are ***amphoteric*** (having both acidic and basic properties).

α-Amino Acids – Acid-Base Properties

- The predominant form of the amino acid depends on the **pH** of the solution

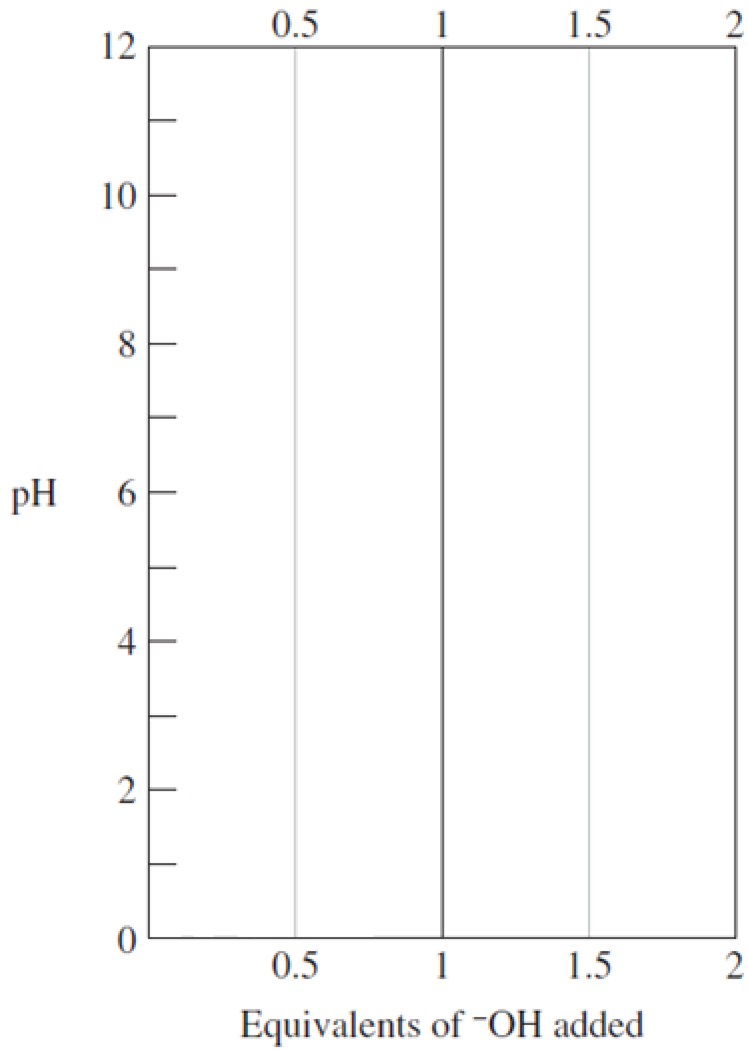


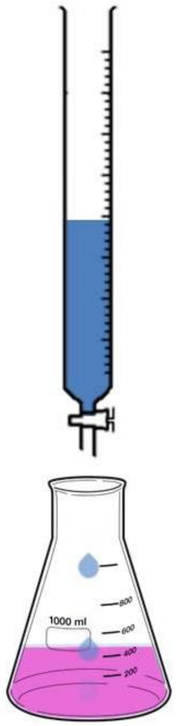
- In an **acidic** solution, the –COO^- group is **protonated** to a free –COOH group, and the molecule has an overall **positive charge**
- As the pH is raised, the –COOH loses its proton and becomes **zwitterion** at about pH 2. This point is called **pK_{a1}**, **the first acid-dissociation constant**
- As the pH is raised further, the –NH_3^+ group loses its proton at about pH 9 or 10. This point is called **pK_{a1}**, **the second acid-dissociation constant**. Above this pH, the molecule has an overall **negative charge**

α-Amino Acids – Acid-Base Properties

- **Titration curve for glycine**;

Isoelectric point (pI) is the pH where the amino acid exists in the zwitterionic form

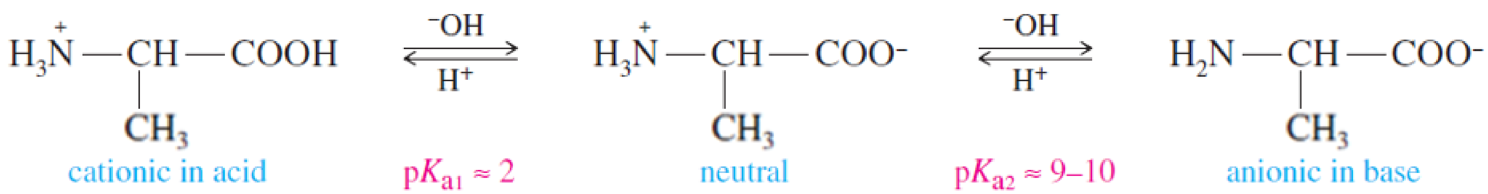




α-Amino Acids – Acid-Base Properties

- Isoelectric pH depends on the amino acid structure

Neutral amino acids: (5.0 to 6.3); **alanine (6.0)**



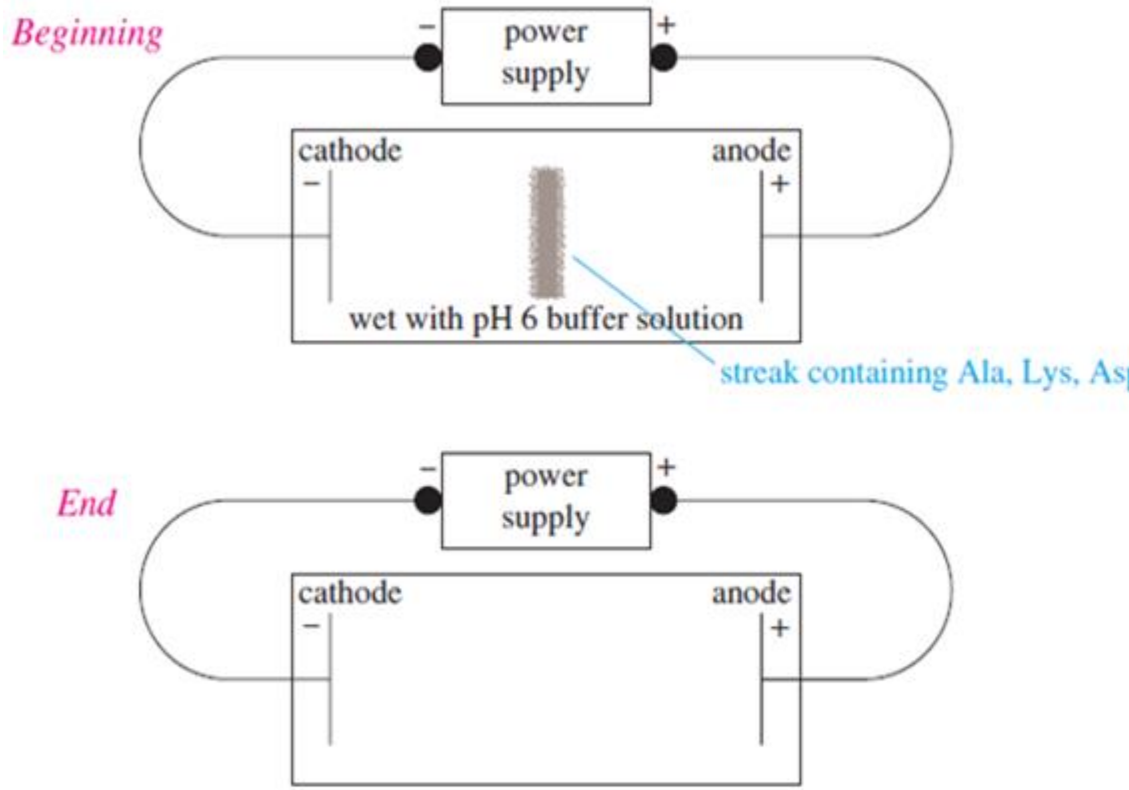
Acidic amino acids: **aspartic acid (2.8)**, glutamic acid (3.2)

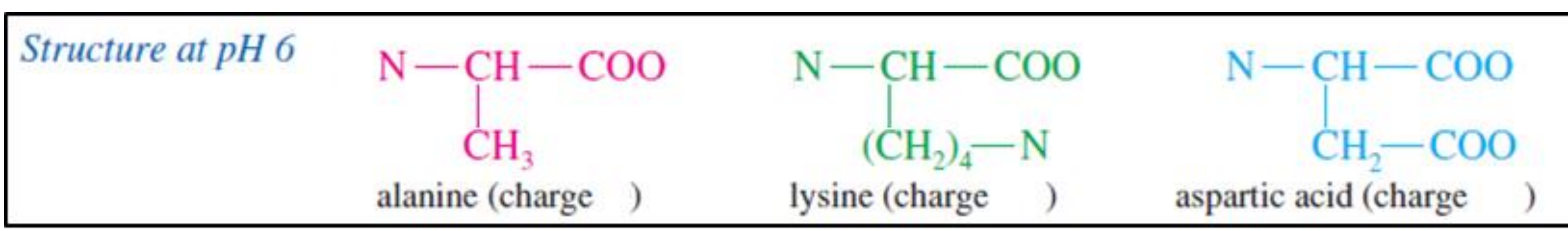
Basic amino acids: **lysine (9.7)**, arginine (10.8), histidine (7.6)

Electrophoresis separate mixtures of amino acids

An amino acid mixture is placed in the centre of a gel. Two electrodes are placed at the edges, and a potential is applied across the electrodes

Positively charged amino acids are attracted to the **negative electrode**, and **negatively charged amino acids** are attracted to the **positive electrode**. An amino acid at its **isoelectric** point has no net charge, so it **does not move**





Key concepts:

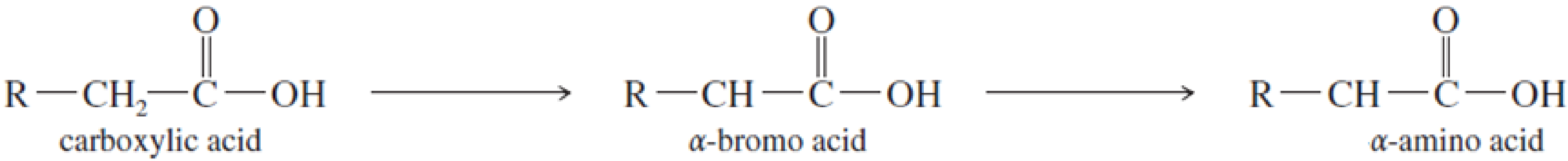
- How can we synthesize amino acids

α-Amino Acids – Synthesis

1) Reductive Amination; formation of amino acids from appropriate ***α*-ketoacid**

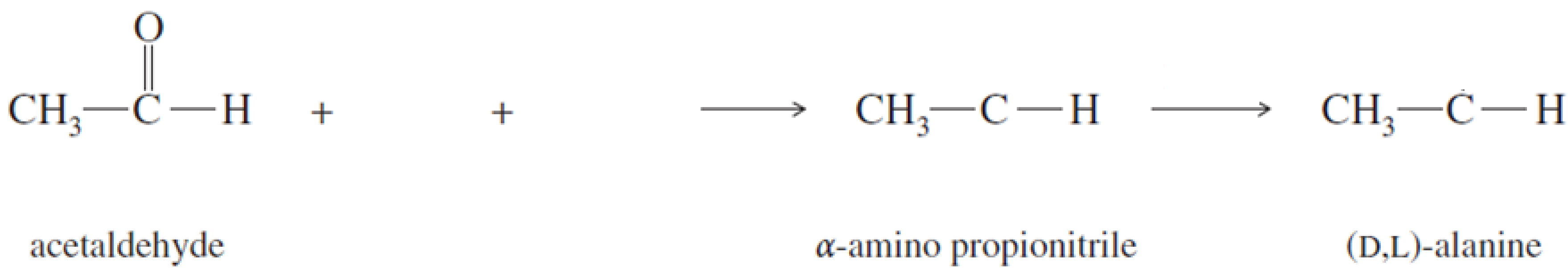
α-Amino Acids – Synthesis

2) S_N2 Amination of ***α*-haloacid**



α-Amino Acids – Synthesis

3) The Strecker Synthesis; formation of amino acids from appropriate **aldehydes**



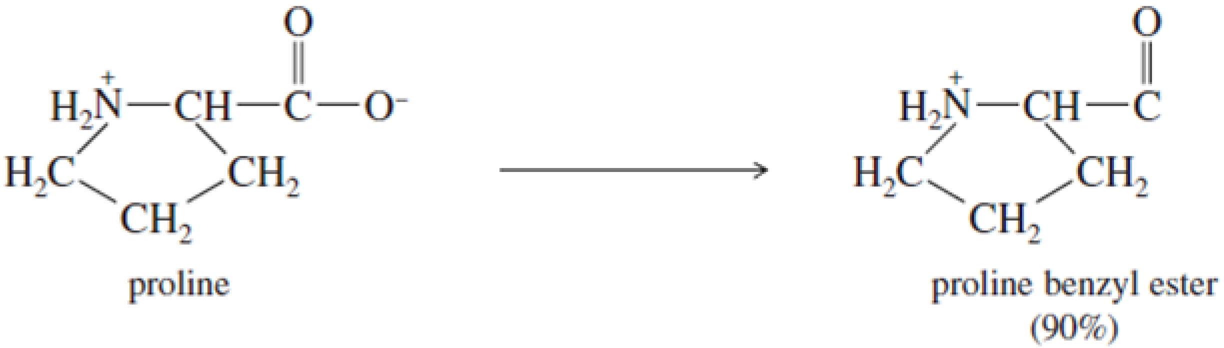
Key concepts:

- How can we modify the structure of amino acids

α-Amino Acids – Reactions

1) Esterification of the Carboxyl Group

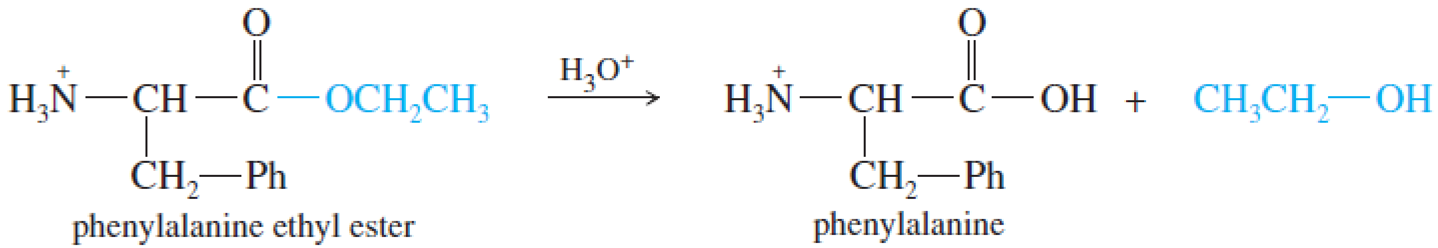
- Like other carboxylic acids, amino acids are **esterified** by treatment with a large excess of an **alcohol** and an **acidic catalyst**; Under acidic conditions, the amino group is present in its protonated form, so it does not interfere with esterification



α-Amino Acids – Reactions

1) Esterification of the Carboxyl Group

- Esters of amino acids are often used as **protected derivatives** to prevent the carboxyl group from reacting in some undesired manner
- **Aqueous acid** hydrolyses the ester and **regenerates the free amino acid**



α-Amino Acids – Reactions

2) Acylation of the Amino Group – Formation of Amides

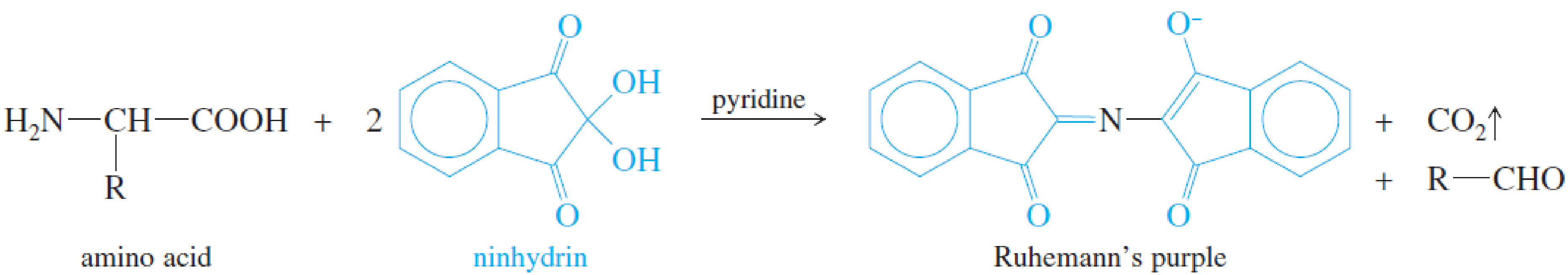
- **Acylating agent** (acid chloride/anhydride) converts the amino group to an **amide**

α-Amino Acids – Reactions

3) Reaction with Ninhydrin

- Ninhydrin is a common reagent for **visualizing** spots or bands of amino acids that have been separated by chromatography or electrophoresis

Reaction of an amino acid with ninhydrin



- When ninhydrin reacts with an amino acid, one of the products is a deep violet, resonance-stabilised anion called **Ruhemann's purple**
- Ninhydrin produces this same purple dye regardless of the structure of the original amino acid
- The side chain of the amino acid is lost as an **aldehyde**