Enzymes Nomenclature

I : shortnames – recommended + convenient

- substrate + "ase"
  e.g. glucosidase, urease, sucrase
- "ase" added to description of the action
  lactate dehydrogenase, adenyl cyclase
- trivial names
  trypsin, pepsin

II Systematic name

Enzyme Commission (EC) of the IUBMB classified enzymes into six major groups according to type of reaction catalyzed. The suffic ase is added to a fairly complete description of the chemical reaction catalyzed

e.g. D-glyceraldehyde 3-phosphate:NAD oxidoreductase

glucokinase (common name)

ATP: D-hexose 6-phosphotransferase

EC number is: (EC 2.7.1.2)

2 → EC number class (transferase)

7 → no. of subclass for transfer of phosphorus-containing group

1 → refers to transfer to an alcoholic acceptor (sub subclass)

2 → specific number of the enzyme

1. Oxidoreductases

- Very common reactions and a broad class

- e.g. dehydrogenases
  accepts or donate hydride ions or hydrogen atoms

- i hydroxylases } → [O_2 → acceptor ; → Water] | Requires metal ion
  ii Oxidases } → [or O_2 → Water]
  iii Oxygenase $\underbrace{O_2}_{\text{both}}$ → acceptor

$$CH_3CH_2OH + NAD^+ \xrightarrow{AD} CH_3\overset{O}{\overset{\|}{C}}-H + NADH + H^+$$

2. Transferases

Catalyze transfer of C-, N- or P-containing groups.

e.g.
- Kinase : transfer of ~P
- glycosyl transferase : carbohydrate residue
- acyl transferase : fatty acyl group
- Aminotransferase or transaminases
- Syntheses : synthesis of physiologically impt. compd. e.g. G.S.

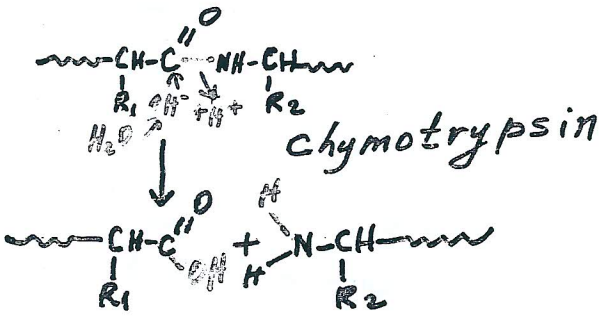
good leaving group

Asp $^{-}OOC-\overset{NH_3^+}{\overset{|}{C}}H-CH_2-COO^-$ + α-KG $^{-}OOC-\overset{O}{\overset{\|}{C}}-CH_2-CH_2-COO^-$ $\xrightleftharpoons[\text{Aminotransferase}]{PLP}$ $^{-}OOC-\overset{O}{\overset{\|}{C}}-CH_2-COO^-$ O.A. + $^{-}OOC-\overset{NH_3^+}{\overset{|}{C}}H-CH_2-CH_2-COO^-$ Glu

3- Hydrolases

Cleavag of C-O, C-N or C-S bonds by addition of water as OH^- and H^+

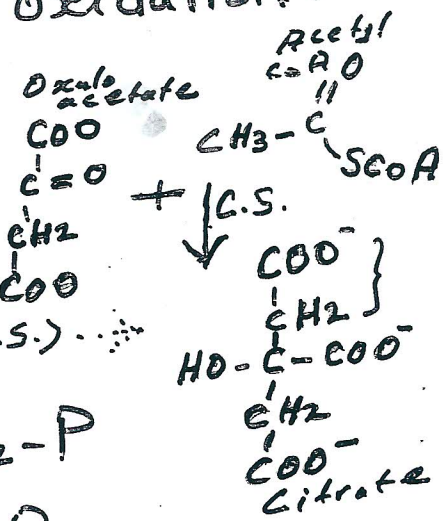
e.g. Proteases

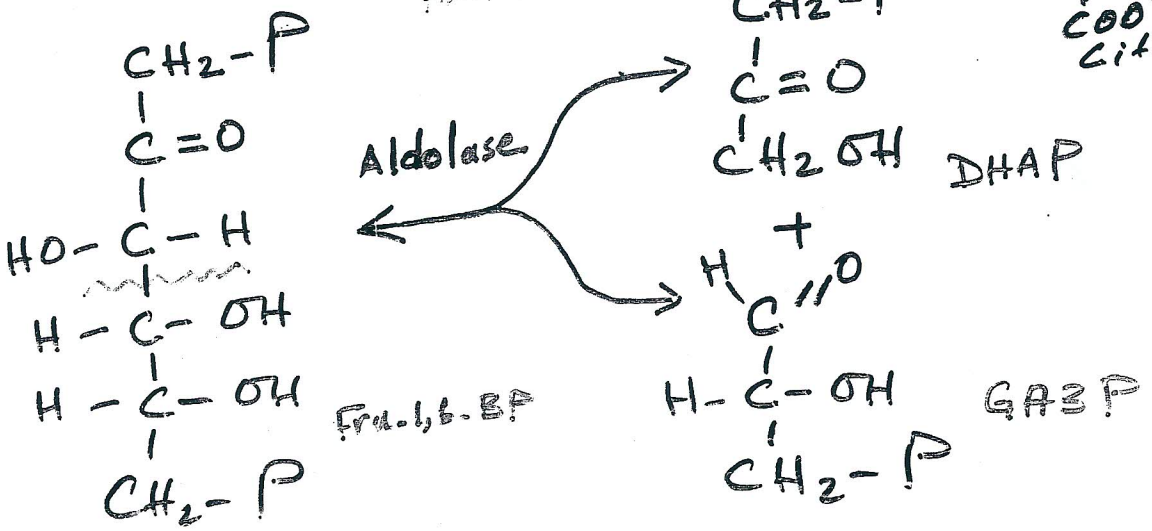


4- Lyases

Cleavage of C-C, C-O & C-N bonds by means other than hydrolysis or oxidation.

Aldolases
decarboxylases
thiolases
Dehydratases
Some synthases (C.S.)





5- Isomerases

Isomerases — rearranging bond structures (e.g. optical, geometrical isomers)

e.g. Mutases G6P ⟷ G-1-P

e.g. DHAP (ketotriose) $\xleftrightarrow{\text{Isomerase}}$ GA3P (aldotriose)

6- Ligases

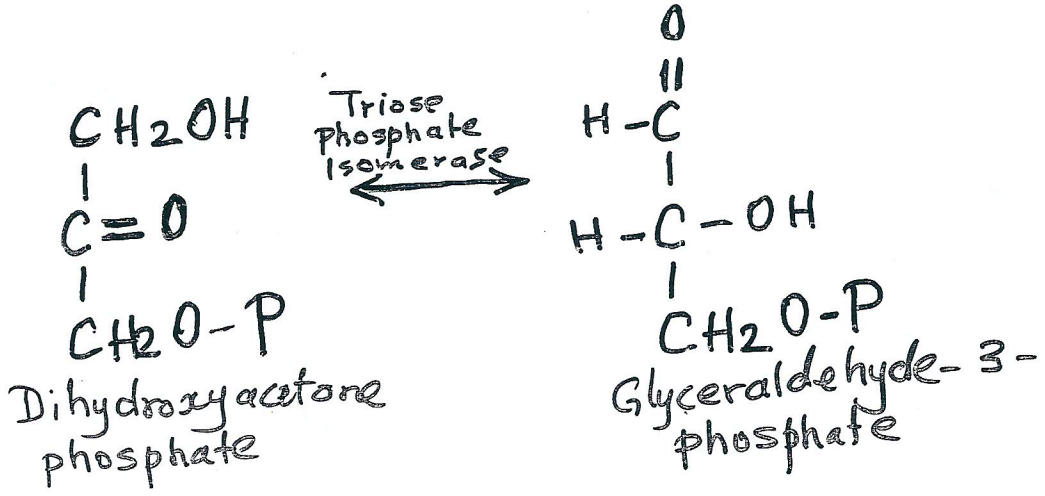
synthesize C-C, C-S, C-O & C-N bonds coupled to cleavage of high energy phosphate bond

e.g. Carboxylases: Add CO_2, require biotin

Synthetases — to be distinguished from synthases.

Synthetase are different from synthase under "Lyases" and "Transferases" as they derive energy from ATP

e.g. for isomerase



Enzymes

- Historical Background

I. Enzyme Catalyzed Reaction

$$E + S \rightleftharpoons ES \rightleftharpoons EP \rightleftharpoons E + P$$

- Enzymes are Proteins (Exception Ribozymes)
- High Catalytic Power
  increase rate by 10^6 to 10^{14}-fold
- High Specificity
- Enzymes are Regulated

A. The Active site

- 3-dimensional structure
- Role of functional groups, cofactors
- Transition state

B. Substrate Binding site

1. Lock-and-key Model
2. Induced-fit Model

C. The Transition State Complex

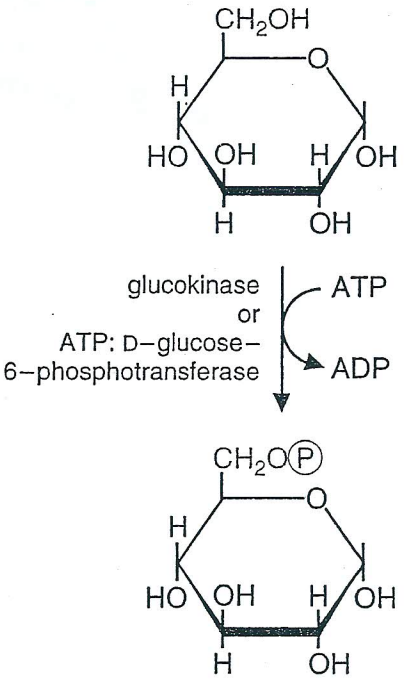
Active Sites of Enzymes Have Some Common Features :-

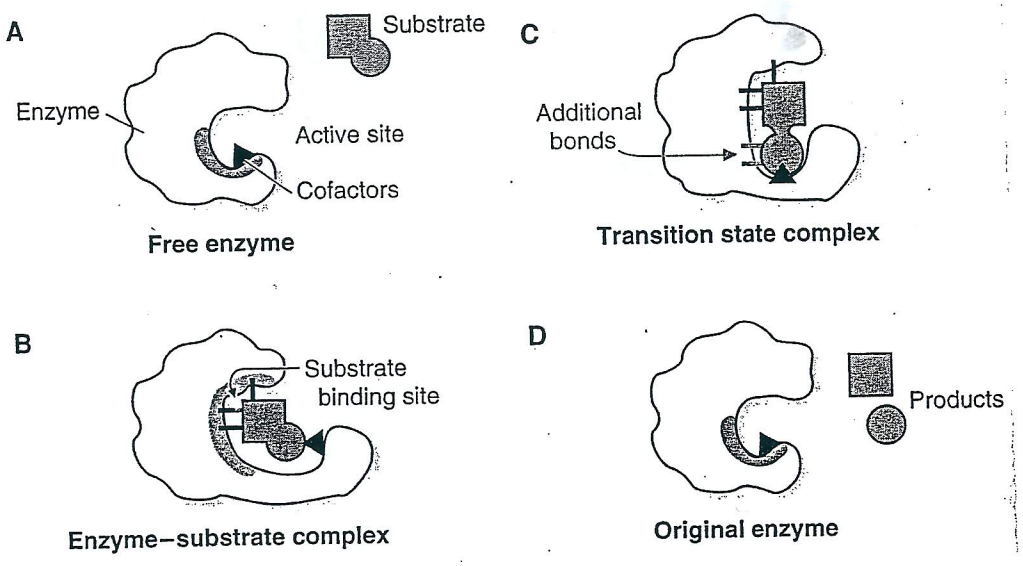
- The catalytic groups
- The active site takes up a relatively small part of the total volume of an enzyme
- The active site is a three-dimensional entity formed by groups that come from different parts of the linear amino-acid sequence
- substrates are bound to enzymes by multiple weak interactions.
- Active sites are clefts or crevices
- The specificity of binding depends on the precisely defined arrangements of atoms in an active site

Emil Fisher's Lock & Key model

Koshland's Induced Fit model

The Active site

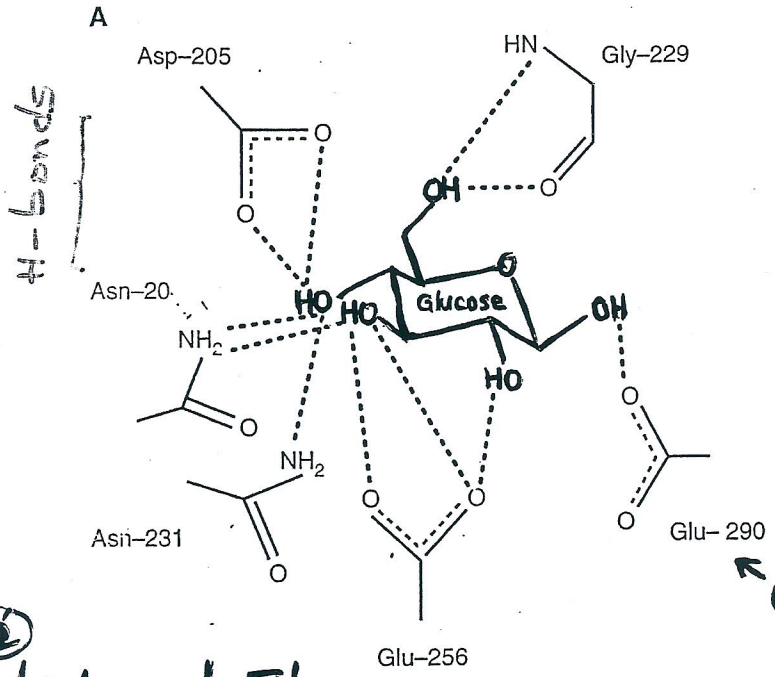


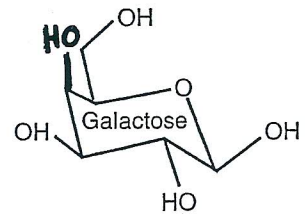


B- Substrate Binding sites

3

- hydrophobic
- Electrostatic
- H-bonds

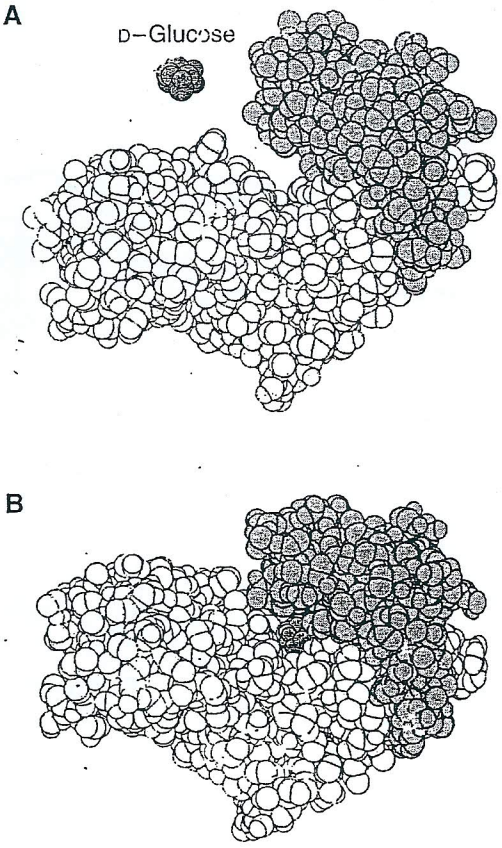




① Lock-and-key model for substrate binding

② Induced Fit Model

Yeast HK →



C- The Transition State Complex

Enzymes Accelerate Reactions by Stabilizing Transition States.

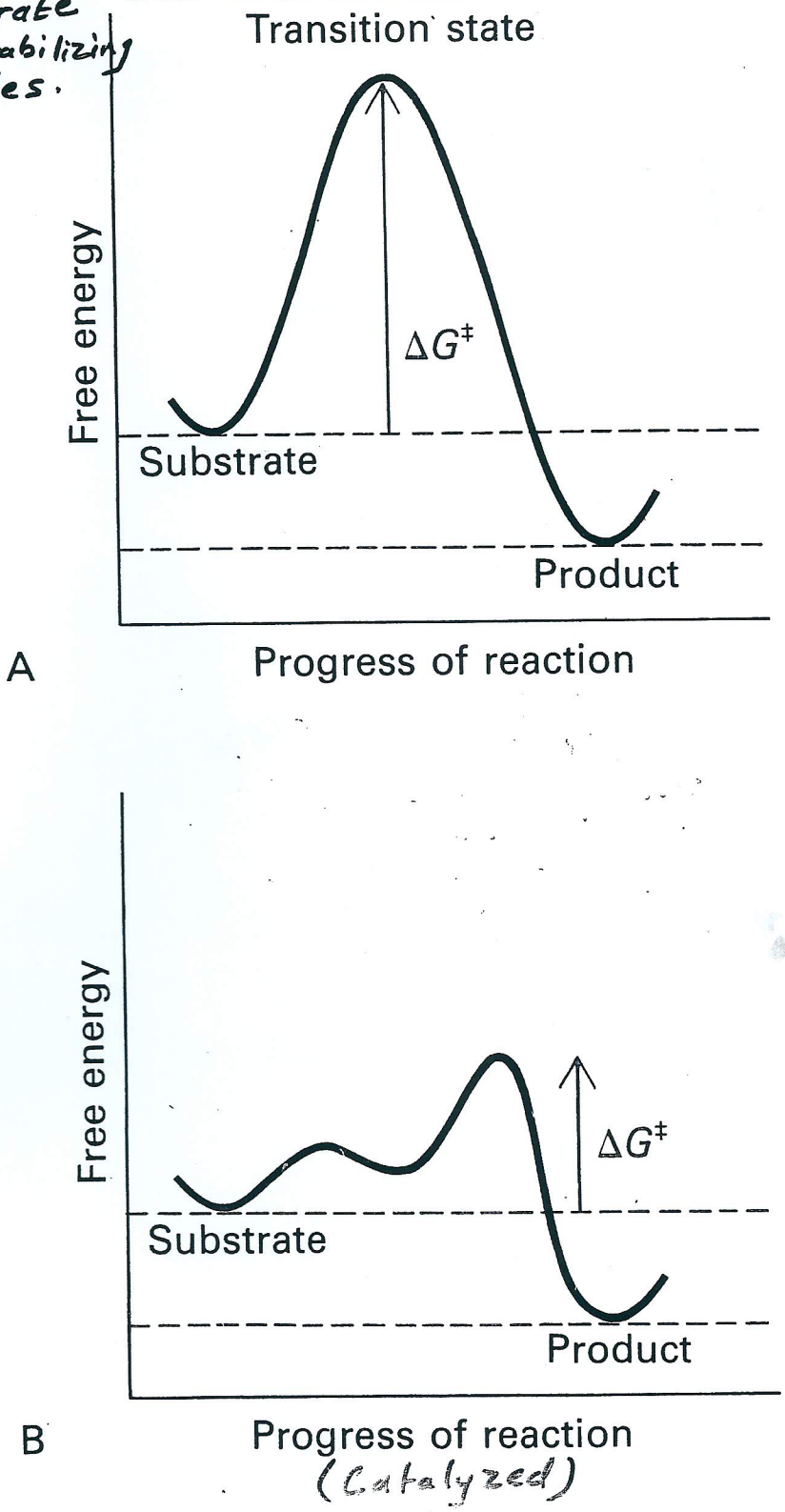


Figure 8-8

Stryer: *Biochemistry*, Third Edition

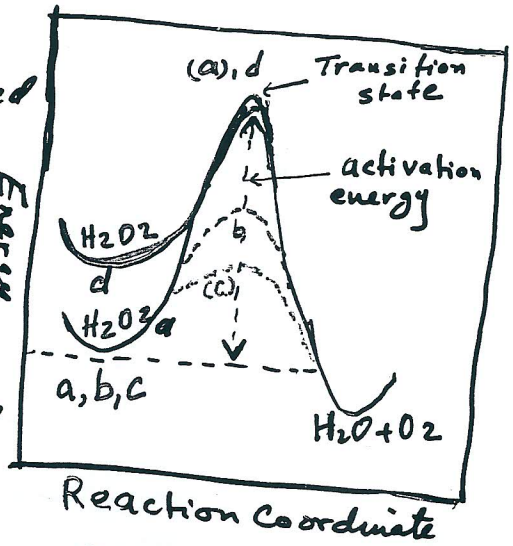
The energy diagram for the decomposition of $H_2O_2 \longrightarrow H_2O + O_2$ 4b

Curve a :- uncatalyzed

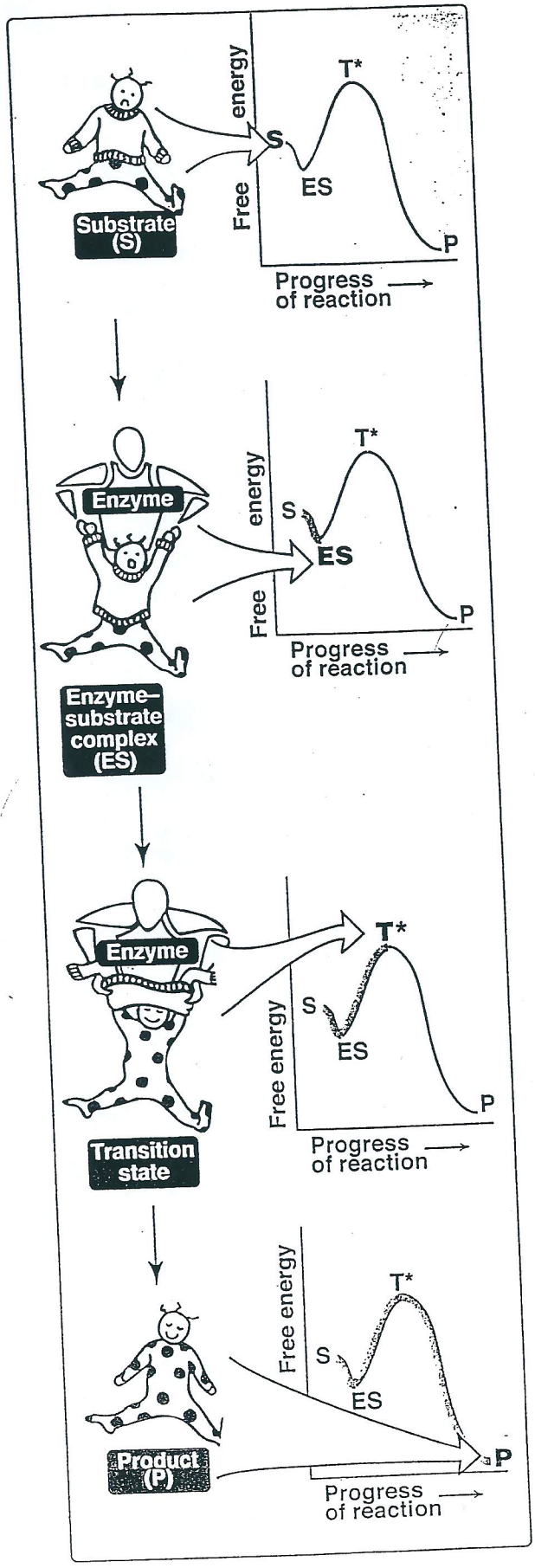
Curve b :- + iron catalyst ↑ 30,000

Curve c: + Catalase ↑ 100,000,000

Curve d : uncatalyzed but at elevated temp



$2H_2O_2 \rightleftharpoons 2H_2O + O_2$


Substrate (S)
Free energy
T*
S
ES
P
Progress of reaction
Enzyme
Enzyme–substrate complex (ES)
Free energy
T*
S
ES
P
Progress of reaction
Enzyme
Transition state
Free energy
T*
S
ES
P
Progress of reaction
Product (P)
Free energy
T*
S
ES
P
Progress of reaction

II Functional Groups in Catalysis

Mechanism of Enzyme Action Involves

- Proximity and Orientation - All
- Electrostatic Interaction to stabilize transition state - All
- Covalent intermediates - some

Enzymes Employ:-

A. Functional groups of Amino Acid side chains

All polar amino acids are involved e.g. Ser, Cys, Lys, His

B. Coenzymes in Catalysis

→ Provides functional groups

→ Made from vitamins

- 1 Activation-Transfer-Coenzymes

Functional gr. of Coenzyme binds covalently to [S], another portion binds tightly to [E]

2 Oxidation-Reduction Coenzymes

Enzyme-cofactors

Difinition

Apoenzyme + Cofactor = Holoenzyme

Cofactors

- small org. molecules (coenzymes)
  - Tightly bound (prosthetic group)
  - loosely bound (co-substrate)
- Met. org
- metals

Coenzymes

Activation - transfer coenzymes

- Thiamine Pyrophosphate
- FAD
- NAD^+

Ox-Red Coenzymes

- Pyridoxal phosphate
- Co A
- Biotin
- Tetrahydrofolate
- B12

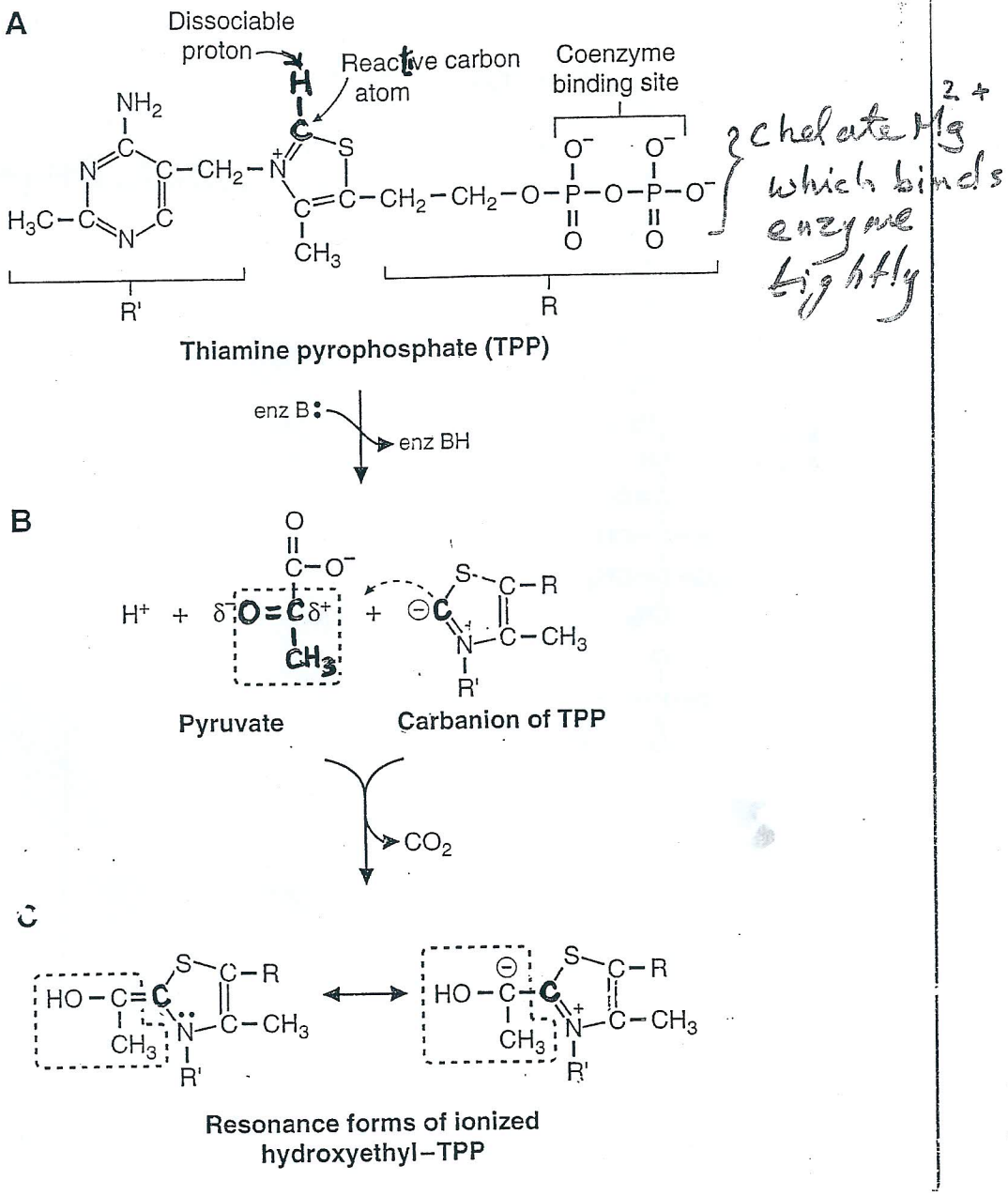
Metals

- Zn^{2+}
- Mg^{2+}
- Ni^{2+}
- Mo
- Se
- Mn^{2+}
- K^+

Table 8.1. Some Functional Groups in the Active Site

Function of Amino Acid	Enzyme Example
Coyalent intermediates	
Cysteine–SH	Glyceraldehyde 3–phosphate dehydrogenase
Serine–OH	Acetylcholinesterase
Lysine–NH_2	Aldolase
Histidine–NH	Phosphoglucomutase
Acid–base catalysis	
Histidine–NH	Chymotrypsin
Aspartate–COOH	Pepsin
Stabilization of anion formed during the reaction	
Peptide backbone–NH	Chymotrypsin
Arginine–NH	Carboxypeptidase A
Serine–OH	Alcohol dehydrogenase
Stabilization of cation formed during the reaction	
Aspartate–COO^-	Lysozyme

Thiamine Pyrophosphate

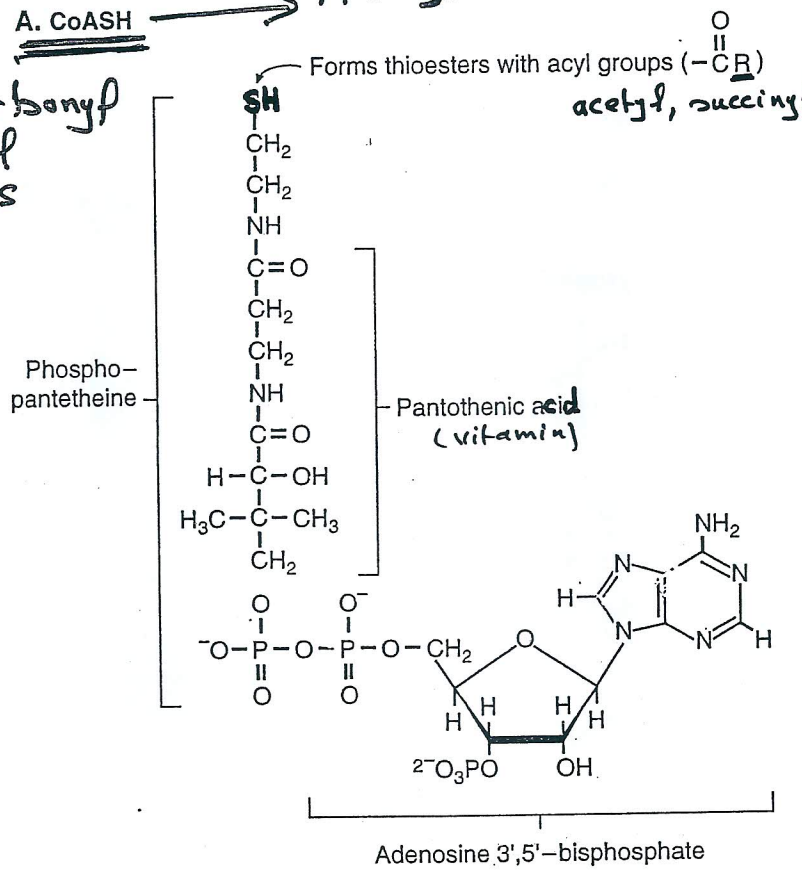


CoA — A stands for the acyl group that becomes attached

Acetyl CoA

A. CoASH

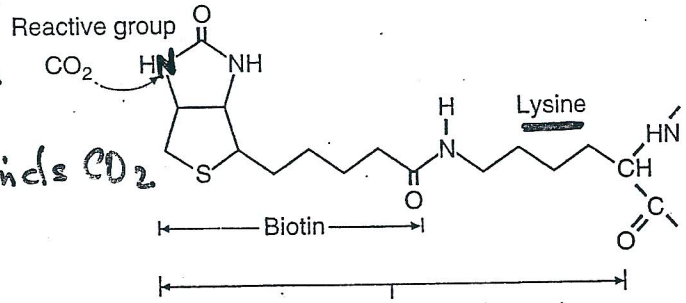
attacks carbonyl groups → acyl thioesters



B. Biotin

Carboxylation

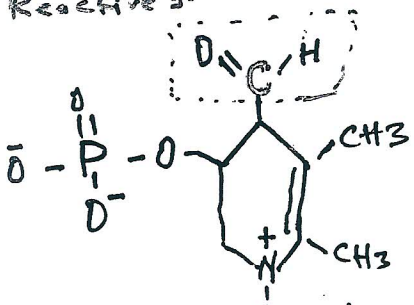
Covalently binds CO_2



Enzyme in Carboxylase enzyme

Pyridoxine

Reactive 3°

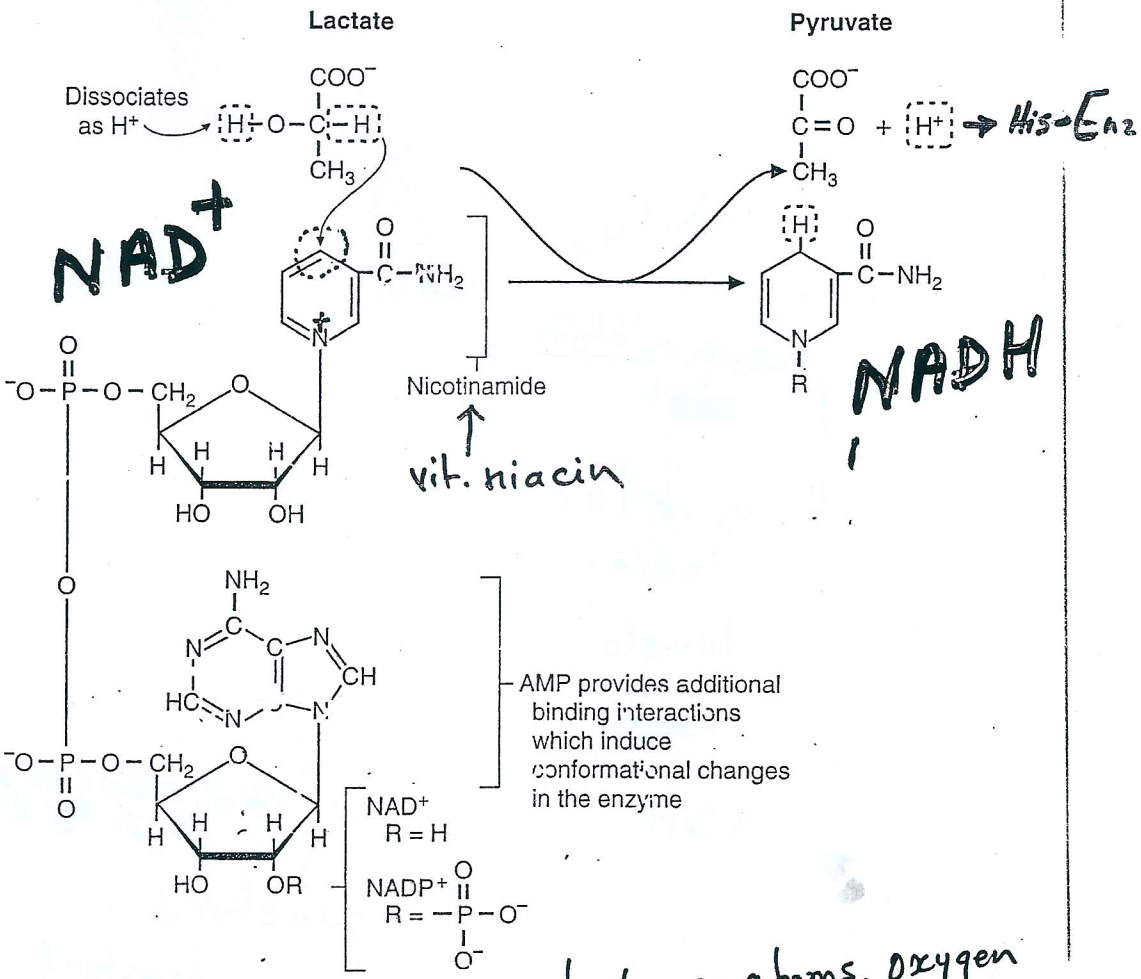


Pyridoxal phosphate

forms covalent intermediate with amino gr. of amino acids

Pyridoxine (Vit B6)

Oxidation-Reduction Coenzymes
NAD^+ ($NADP^+$)

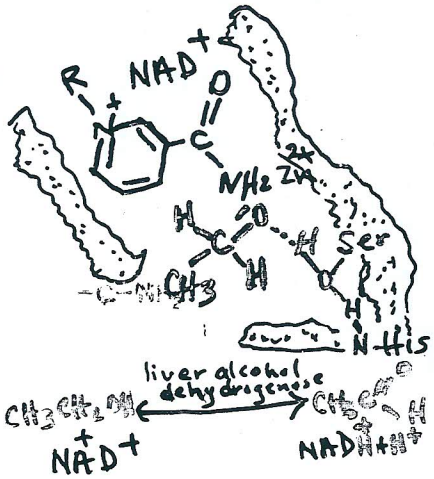


- Transfers Hydride ions, hydrogen atoms, oxygen
- No covalent intermediates
- Require participation of amino groups of [E]
- Unique roles in generation of ATP
- Some work with metal to transfer $\bar{e}$

Other Coenzymes: Vit E + C are ox-red coenzymes — Antioxidants

$$FAD + 2H \longrightarrow FADH_2$$

C. Metal Ions in Catalysis



Metal ions act as electrophiles

- they assit in binding of substrates
- stabilize developing anions

e.g. Mg^{2+} in binding ATP, TPP

Zn^{2+} in ADH

- electron transport in Ox-Red. reactions e.g. cyt.

D. Non Catalytic Roles of Cofactors

- binding different regions → tert. structure
- serve as [S], cleaved during reaction

III Optimal pH and Temp.