EXTRA CREDIT PAPER

Due date : April 15

Length : 5-7 pages

# of sources : 5 or more

Format :
- summary
- introduction
- discussion
- conclusions or future research
- references

Credit : up to 50 pts

Oral presentation : 10-12 minutes

* the approach to the topic should be BIOCHEMICAL

Some paper topics:

- Urey-Miller experiment
- Scurvy
- Prion diseases
- Enzyme inhibitors as drugs
- Structure of DNA
- Sickle cell anemia
- HIV enzyme inhibitors
- DNA sequencing
- Hemoglobin Type C
- Mad cow disease
- IgG structure
- Buffers
- Glycogen storage diseases
- Low carbohydrate diets
- Cystic fibrosis
- Ribonuclease A
- Protein structure prediction
- Chemical basis of penicillin resistance
- IgE & allergic reactions
- Isomerases & chaperones in protein folding
- Lactoferrin
- Serotonin
- Chemotrypsin
- Lactase deficiency
- Glycogen (carbo) loading in athletes

$$A + B \rightleftharpoons C + D$$

$$\Delta G = \Delta G^{\circ} + RT \log_e \frac{[C][D]}{[A][B]}$$

At equilibrium, $\Delta G = 0$

$$0 = \Delta G^{\circ'} + RT \log_e \frac{[C][D]}{[A][B]} \Rightarrow$$

$$\Delta G^{\circ'} = -RT \log_e \frac{[C][D]}{[A][B]}$$

Equilibrium constant under standard conditions $K'_{eq} = \frac{[C][D]}{[A][B]}$

$$\Delta G^{\circ'} = -RT \log_e K'_{eq}$$

$$\Delta G^{\circ'} = -2.303\, RT \log_{10} K'_{eq}$$

Dihydroxyacetone phosphate

Glyceraldehyde 3-phosphate

At equilibrium, $\frac{[\text{Glyceraldehyde 3-phosphate}]}{[\text{Dihydroxyacetone phosphate}]} = 0.0475$

(pH = 7, $T = 25^\circ C = 298\ K$)

$$\Delta G^{\circ\prime} = -2.303\ RT \log_{10} K'_{eq}$$

$$= -2.303 \times 1.987 \times 10^{-3} \times 298 \times \log_{10}(0.0475)$$

$$= +1.8\ \text{kcal/mol}$$

$$\Delta G = \Delta G^{\circ\prime} + RT \log_e \frac{3 \times 10^{-6}\ M}{2 \times 10^{-4}\ M}$$

$$= 1.8\ \text{kcal/mol} - 2.5\ \text{kcal/mol}$$

$$= -0.7\ \text{kcal/mol}$$

In many biochemical reactions, the energy of the reactants is converted with high efficiency into a different form.

Enzymes cannot alter reaction equilibria

Enzymes accelerate reactions by stabilizing transition states

Enzymes accelerate reactions by decreasing the Gibbs free energy of activation (Δ G), the activation barrier.

The first step in enzymatic catalysis is the formation of an enzyme- substrate complex (ES)

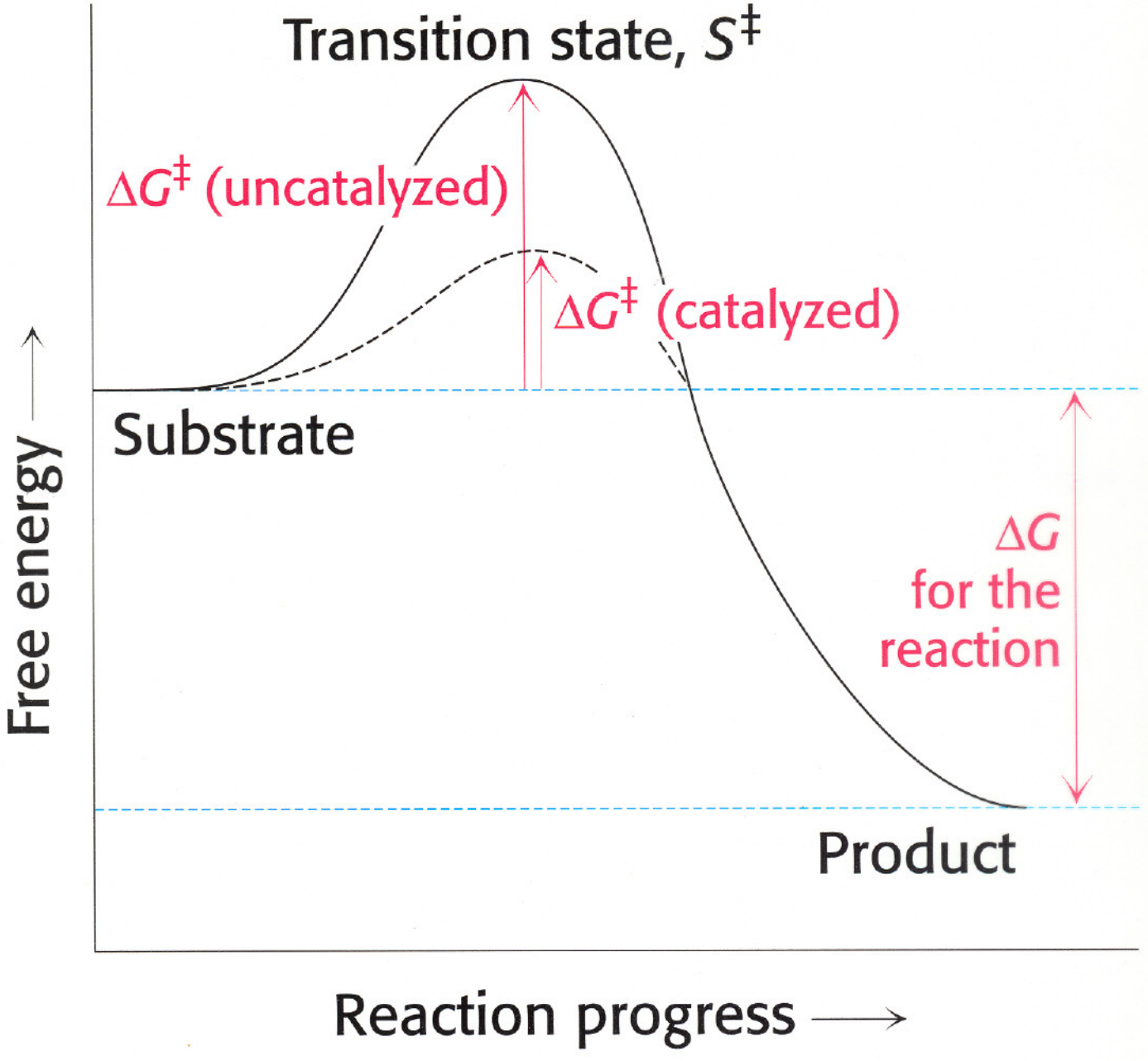


Figure 8-3
Stryer, Tymoczko, & Berg, BIOCHEMISTRY, Fifth Edition.

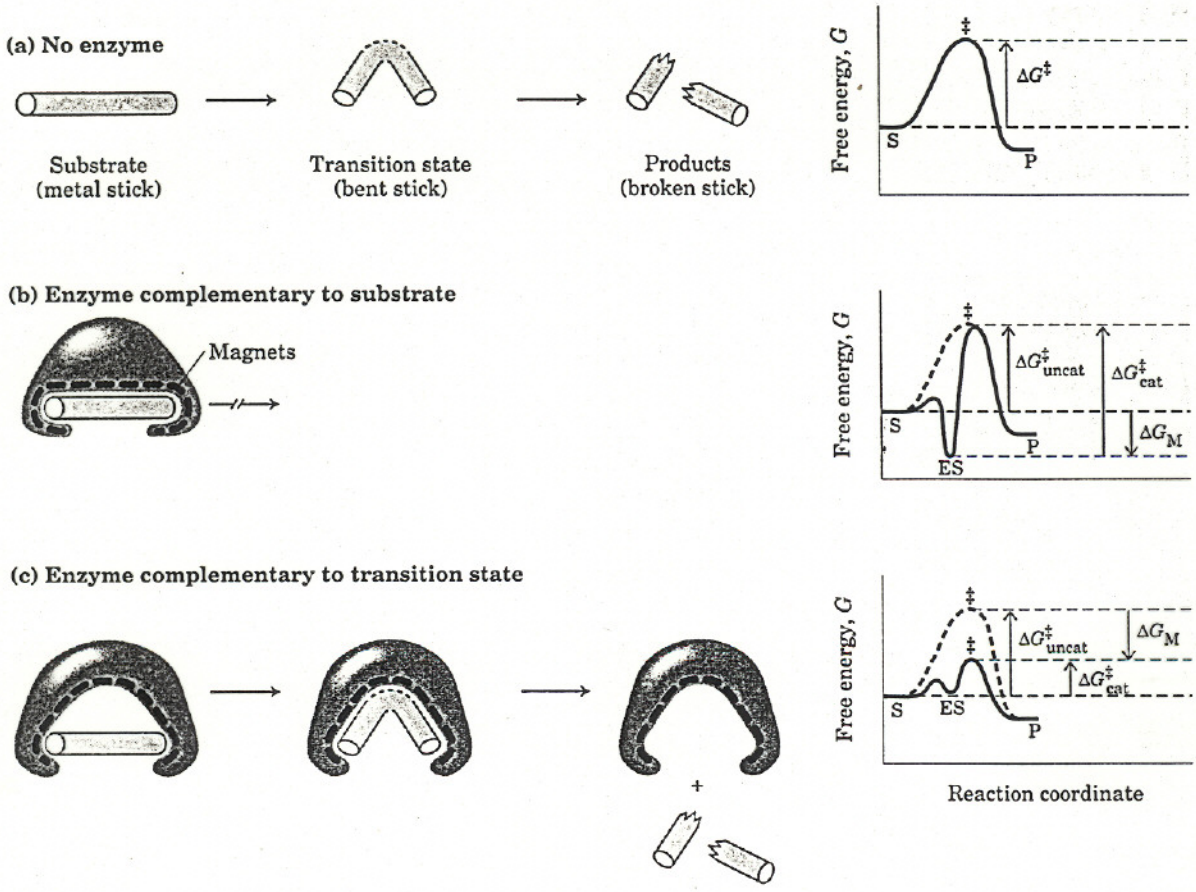


figure 8–5

An imaginary enzyme (stickase) designed to catalyze the breaking of a metal stick. **(a)** Before the stick is broken, it must first be bent (the transition state). In both stickase examples, magnetic interactions take the place of weak-bonding interactions between enzyme and substrate. **(b)** A stickase with a magnet-lined pocket complementary in structure to the stick (the substrate) stabilizes the substrate. Bending is impeded by the magnetic attraction between stick and stickase. **(c)** An enzyme complementary to the reaction transition state helps to destabilize the stick, contributing to catalysis of the reaction. The binding energy of the magnetic interactions compensates for the increase in free energy required to bend the stick. Reaction coordinate diagrams (right) show the energy consequences of complementarity to substrate versus complementarity to transition state (EP complexes are omitted). ΔG_M represents the difference between the transition-state energies of the uncatalyzed and catalyzed reactions, and is contributed by the magnetic interactions between the stick and stickase. When the enzyme is complementary to the substrate **(b)**, the ES complex is more stable and has less free energy in the ground state than substrate alone. The result is an *increase* in the activation energy.

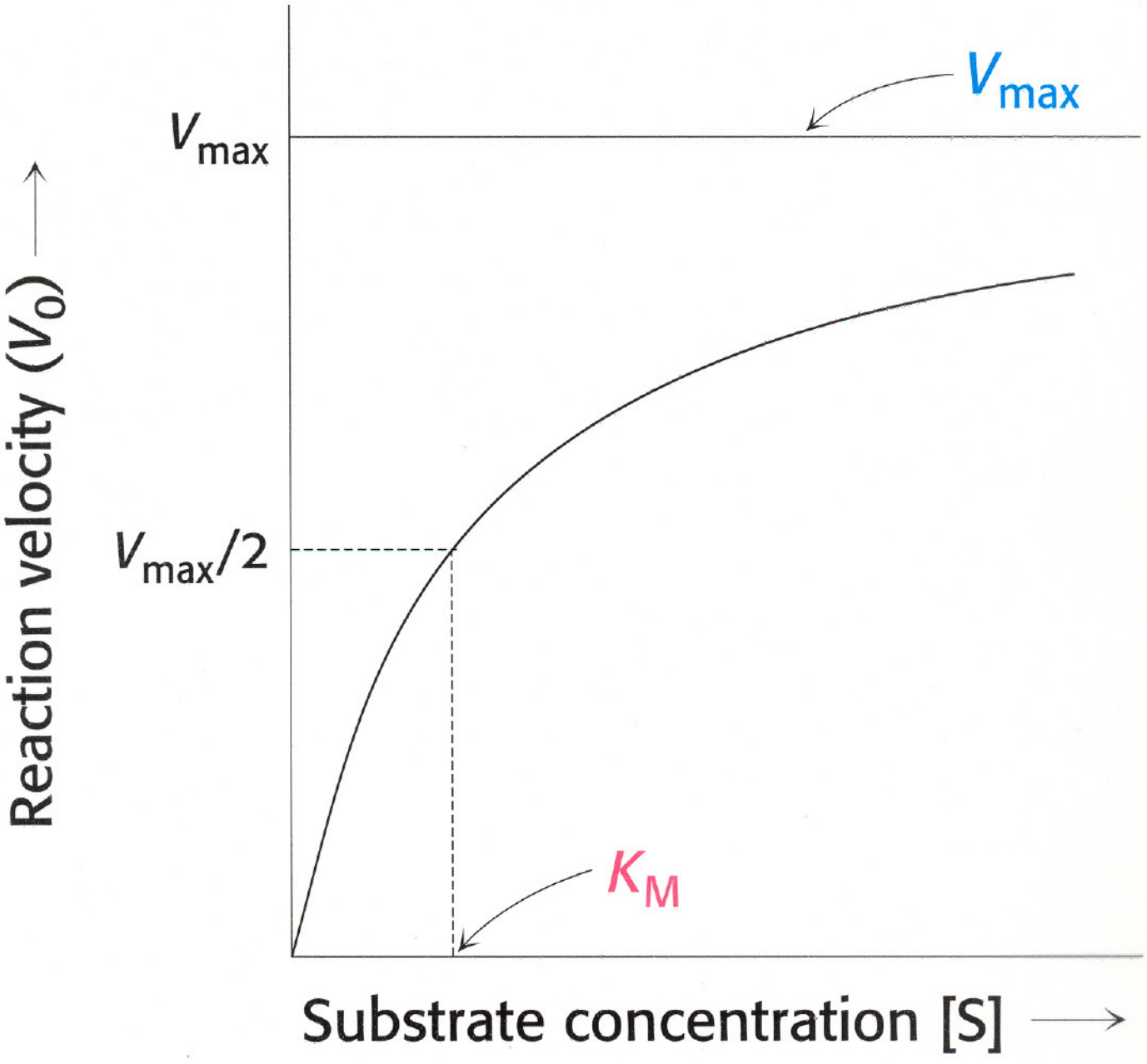


Figure 8-11
Stryer, Tymoczko, & Berg, BIOCHEMISTRY, Fifth Edition.

MICHAELIS - MENTEN EQUATION

$$E + S \underset{k_2}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_3} E + P$$

$$V_o = V_{max} \frac{[S]}{[S] + K_M}$$

K_M is equal to the substrate concentration at which the reaction rate is half its maximal value

So, when $[S] = K_M$ then $V_o = V_{max} / 2$

- At very low substrate concentration, when [S] is much less than K_M, $V_o = \frac{[S] V_{max}}{K_M}$

- At high substrate concentration, when [S] is much greater than K_M, $V_o = V_{max}$

$K_M = 10^{-1} - 10^{-7}\ M$

K_m for Some Enzymes and Substrates

Enzyme	Substrate	K_m (mM)
Catalase	H_2O_2	1100
Hexokinase (brain)	ATP	0.4
	D-Glucose	0.05
	D-Fructose	1.5
Carbonic anhydrase	HCO_3^-	26
Chymotrypsin	Glycyltyrosinylglycine	108
	N-Benzoyltyrosinamide	2.5
β-Galactosidase	D-Lactose	4.0
Threonine dehydratase	L-Threonine	5.0

Enzyme	Substrate	K_M(μM
Chymotrypsin	Acetyl-L-tryptophanamide	5000
Lysozyme	Hexa-*N*-acetylglucosamine	6
β-Galactosidase	Lactose	4000
Threonine deaminase	Threonine	5000
Carbonic anhydrase	CO_2	8000
Penicillinase	Benzylpenicillin	50
Pyruvate carboxylase	Pyruvate	400
	HCO_3^-	1000
	ATP	60
Arginine-tRNA synthetase	Arginine	3
	tRNA	0.4
	ATP	300

Enzyme Inhibition

- Enzyme inhibition serves a major control mechanism in biological systems

- Many drugs and toxins act as enzyme inhibitors

- Enzyme inhibition can provide information on the mechanism of enzyme action

Enzyme inhibition can be either reversible or irreversible

Reversible inhibition can be competitive, noncompetitive, or mixed

Allosteric enzymes do not obey Michaelis- Menten kinetics

Transition state analogs are potent inhibitors of enzymes

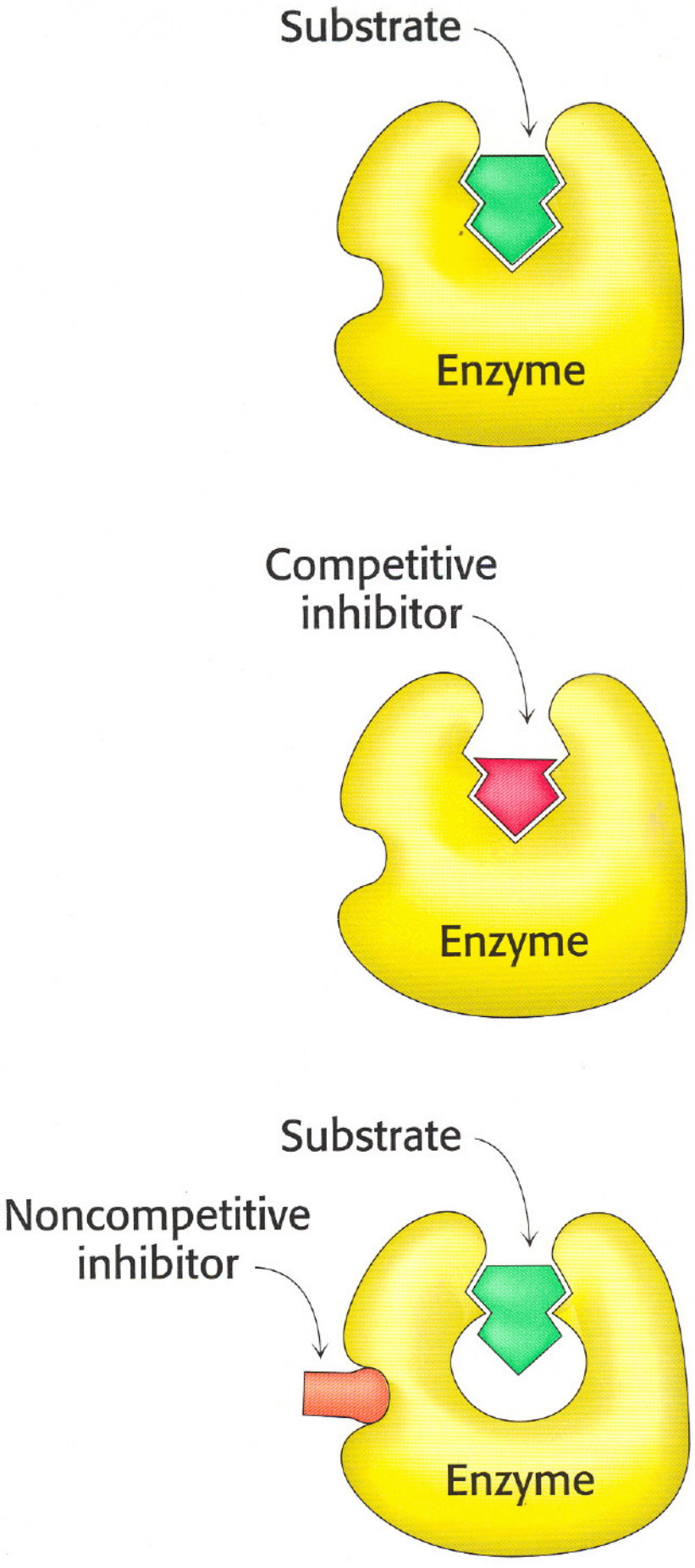


Figure 8-15
Stryer, Tymoczko, & Berg, BIOCHEMISTRY, Fifth Edition.

Catalytic antibodies can be formed by using transition state analogs as immunogens

Lernerd & Schultz (1986) found that catalytic antibodies could be produced by using transition state analogs as immunogens

Transition state analogs can

- **Provide insight into catalytic mechanisms**
- **Serve as potent and specific inhibitors of enzymes**
- **Be used as immunogens to generate a wide range of novel catalysts**

Penicillin and Its Mechanism of Action

Penicillin as discovered by Fleming in 1928

Penicillin blocks the last step in cell wall synthesis by inhibiting transpeptidase irreversibly

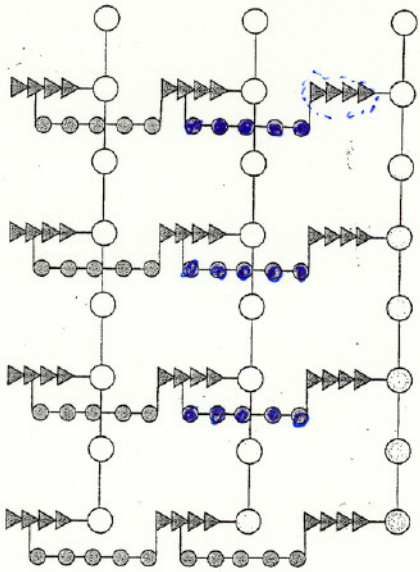


Figure 8-29
Schematic diagram of the peptidoglycan in *Staphylococcus aureus*. The sugars are shown in yellow, the tetrapeptides in red, and the pentaglycine bridges in blue. The cell wall is a single, enormous bag-shaped macromolecule because of extensive cross-linking.

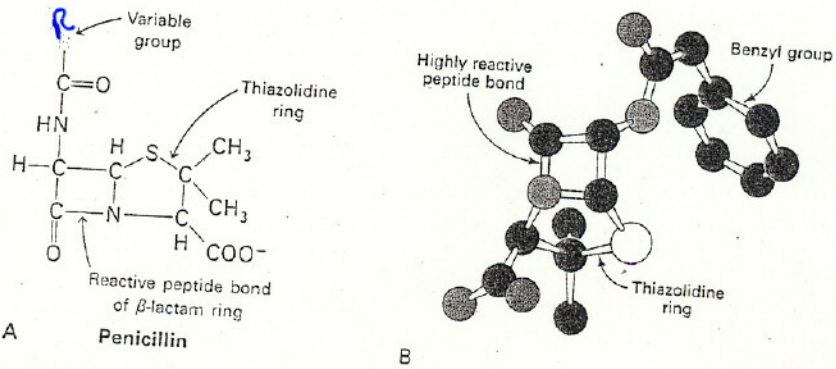


Figure 8-28
(A) Structural formula of penicillin and (B) model of benzyl penicillin. The reactive site of penicillin is the peptide bond of its β-lactam ring.

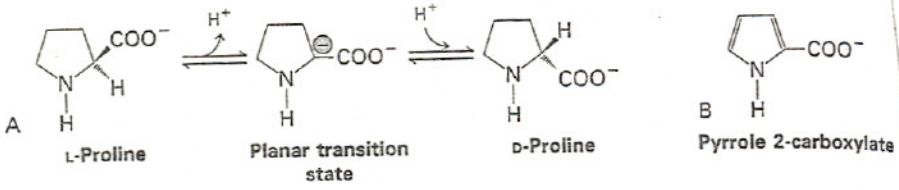


Figure 8-26
(A) The isomerization of L-proline to D-proline by proline racemase, a bacterial enzyme, proceeds through a planar transition state in which the α carbon is trigonal rather than tetrahedral. (B) Pyrrole 2-carboxylate is a transition state analog because it has a planar geometry.

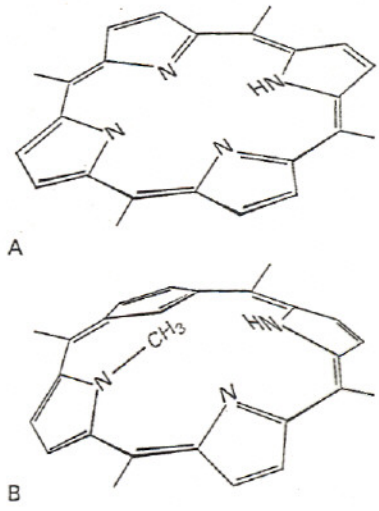


Figure 8-27
(A) The insertion of a metal ion into a porphyrin proceeds through a transition state in which the porphyrin is bent. (B) *N*-methylmesoporphyrin, a bent porphyrin, is an effective immunogen because it resembles the transition state of the reaction.

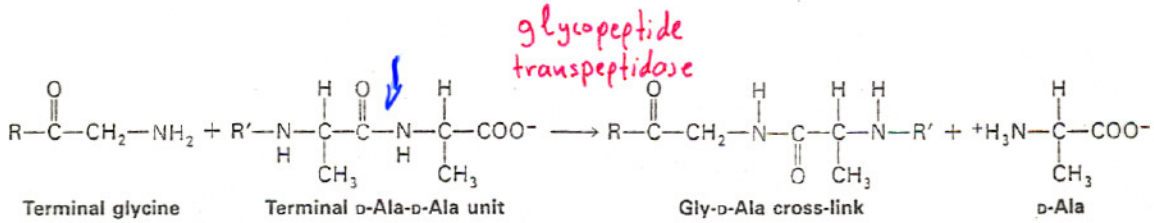


Figure 8-30
The amino group of the pentaglycine bridge in the *S. aureus* cell wall attacks the peptide bond between two D-Ala residues to form a cross-link.

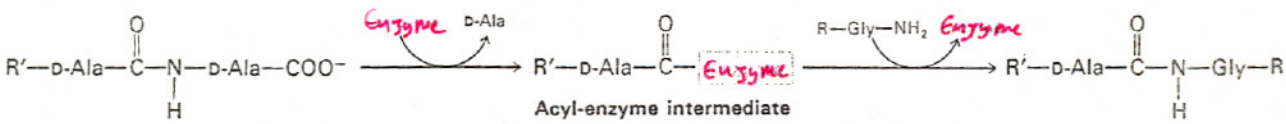


Figure 8-31
An acyl-enzyme intermediate is formed in the transpeptidation reaction.

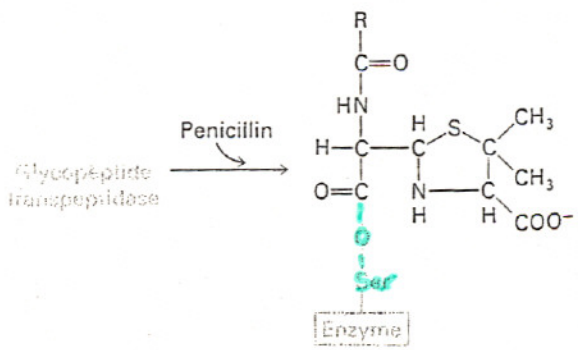
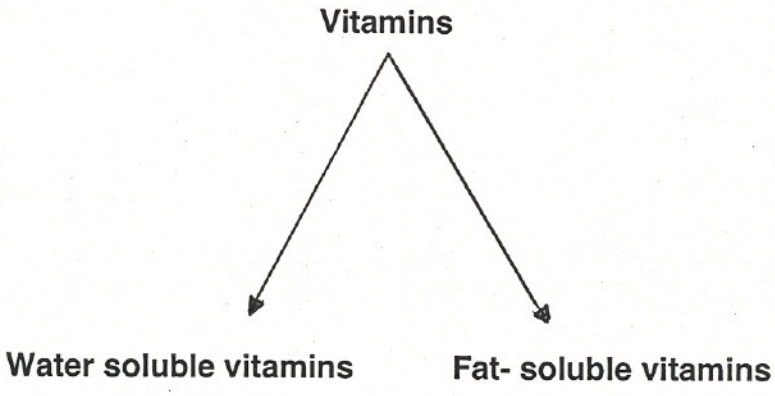


Figure 8-32
Formation of a penicilloyl-enzyme complex, which is indefinitely stable.

VITAMINS

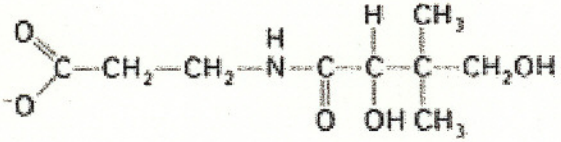
Vitamins are organic molecules that are needed in small amounts in the diets of some higher animals. Higher animals have lost the ability to synthesize them.



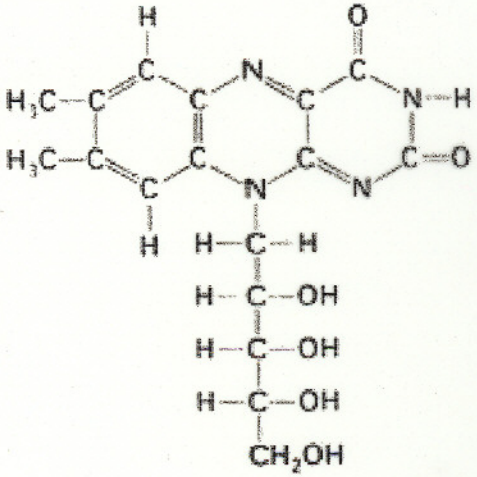
Generally vitamins function as a component of a coenzyme

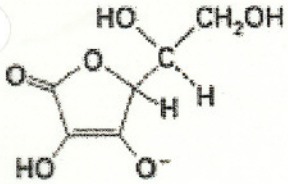
TABLE 8.9 Water-Soluble Vitamins

Vitamin	Coenzyme	Typical reaction type	Consequences of deficiency
Thiamine (B_1)	Thiamine pyrophosphate	Aldehyde transfer	Beriberi (weight loss, heart problems, neurological dysfunction)
Riboflavin (B_2)	Flavin adenine dinucleotide (FAD)	Oxidation–reduction	Cheliosis and angular stomatitus (lesions of the mouth), dermatitis
Pyridoxine (B_6)	Pyridoxal phosphate	Group transfer to or from amino acids	Depression, confusion, convulsions
Nicotinic acid (niacin)	Nicotinamide adenine dinucleotide (NAD^+)	Oxidation–reduction	Pellagra (dermatitis, depression, diarrhea)
Pantothenic acid	Coenzyme A	Acyl–group transfer	Hypertension
Biotin	Biotin–lysine complexes (biocytin)	ATP-dependent carboxylation and carboxyl-group transfer	Rash about the eyebrows, muscle pain, fatigue (rare)
Folic acid	Tetrahydrofolate	Transfer of one-carbon components; thymine synthesis	Anemia, neural-tube defects in development
B_{12}	5′-Deoxyadenosyl cobalamin	Transfer of methyl groups; intramolecular rearrangements	Anemia, pernicious anemia, methylmalonic acidosis
C (ascorbic acid)		Antioxidant	Scurvy (swollen and bleeding gums, subdermal hemorrhages)

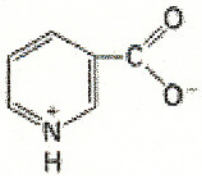


Pantothenate

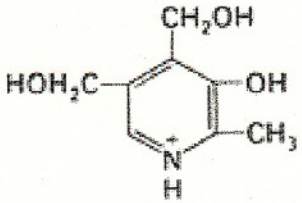




L-Ascorbate
(Vitamin C)



Nicotinate
(Niacin)



Pyridoxine
(A form of vitamin B_6)

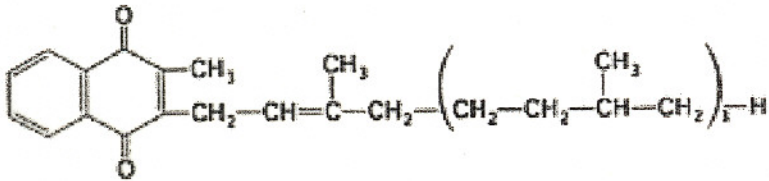
Riboflavin
(Vitamin B_2)

Structures of some water-soluble vitamins

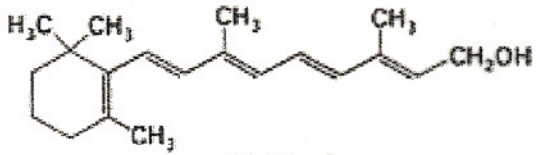
Fig 17-11

TABLE 8.10 Fat-soluble vitamins

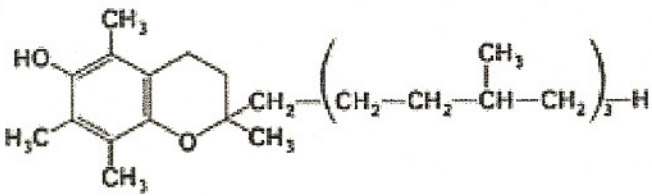
Vitamin	Function	Deficiency
A	Antioxidant	Inhibition of sperm production; lesions in muscles and nerves (rare)
D	Regulation of calcium and phosphate metabolism	Rickets (children): skeletal deformaties, impaired growth Osteomalacia (adults): soft, bending bones
E	Roles in vision, growth, reproduction	Night blindness, cornea damage, damage to respiratory and gastrointestinal tract
K	Blood coagulation	Subdermal hemorrhaging



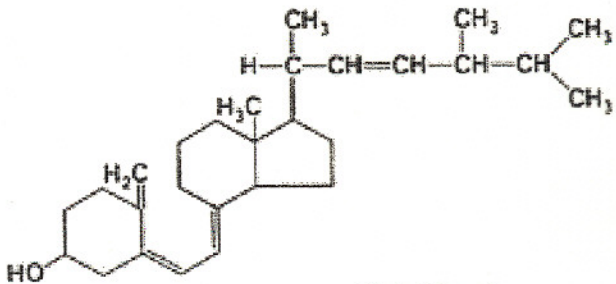
Vitamin K



Retinol
(VitaminA)



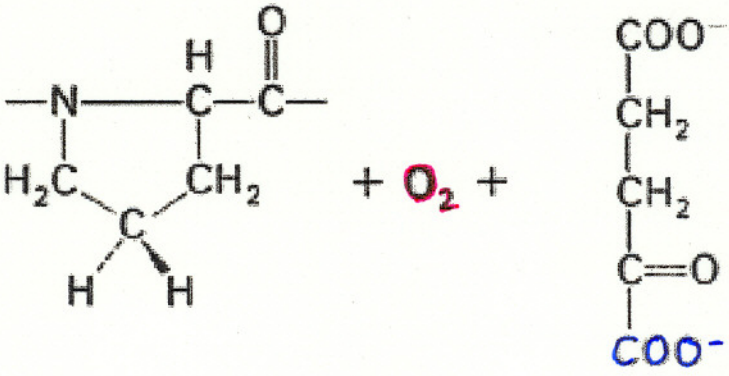
α-Tocopherol
(Vitamin E)



Calciferol
(Vitamin D_2)

Structures of some fat soluble vitamins

Fig 17- 12



Hydroxylation of a proline residue at C-4

Fig 17-13

TABLE 14.2 Some activated carriers in metabolism

Carrier molecule in activated form	Group carried	Vitamin precursor
ATP	Phosphoryl	
NADH and NADPH	Electrons	Nicotinate (niacin)
$FADH_2$	Electrons	Riboflavin (vitamin B_2)
$FMNH_2$	Electrons	Riboflavin (vitamin B_2)
Coenzyme A	Acyl	Pantothenate
Lipoamide	Acyl	
Thiamine pyrophosphate	Aldehyde	Thiamine (vitamin B_1)
Biotin	CO_2	Biotin
Tetrahydrofolate	One-carbon units	Folate
S-Adenosylmethionine	Methyl	
Uridine diphosphate glucose	Glucose	
Cytidine diphosphate diacylglycerol	Phosphatidate	
Nucleoside triphosphates	Nucleotides	

Note: Many of the activated carriers are coenzymes that are derived from water-soluble vitamins (Section 8.6.1).