13.3 Biological oxidation-reduction reactions

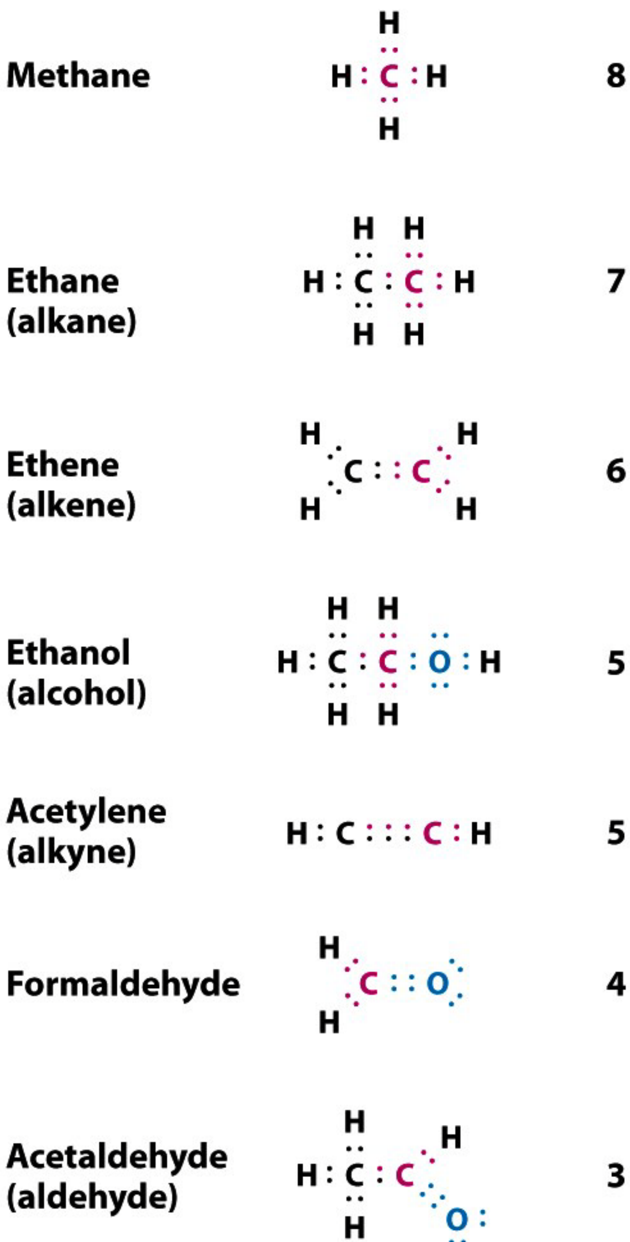
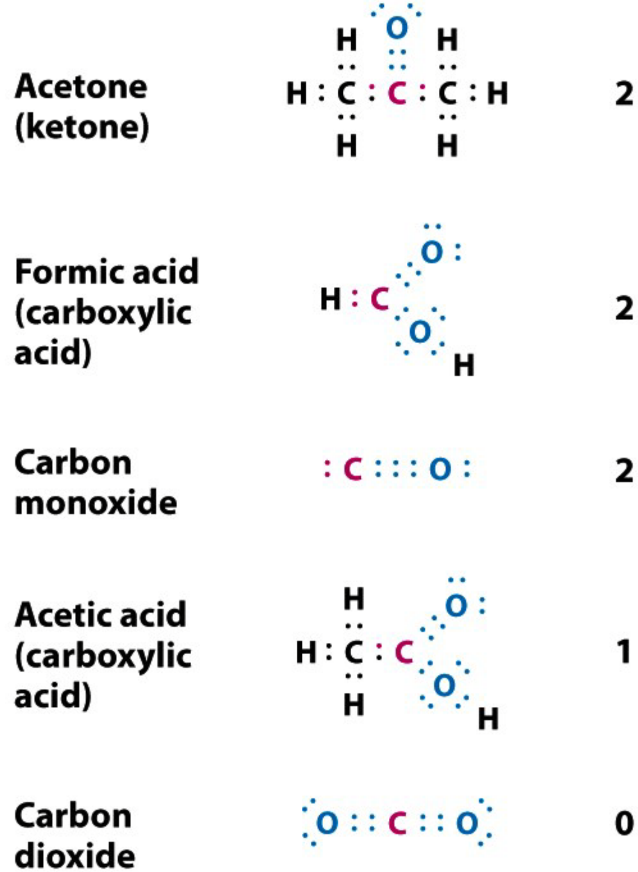


Figure 13-22



Biological oxidation often involve dehydrogenation

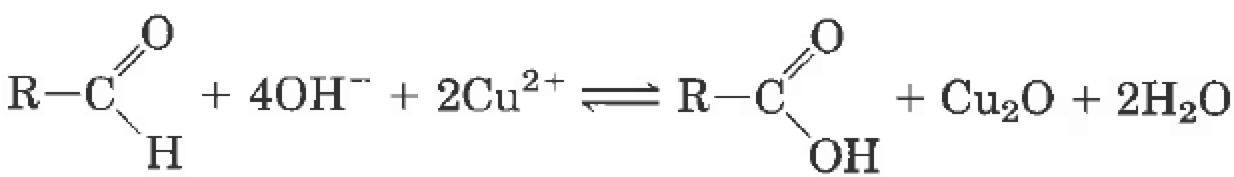
Oxidation-reductions can be described as half-reactions

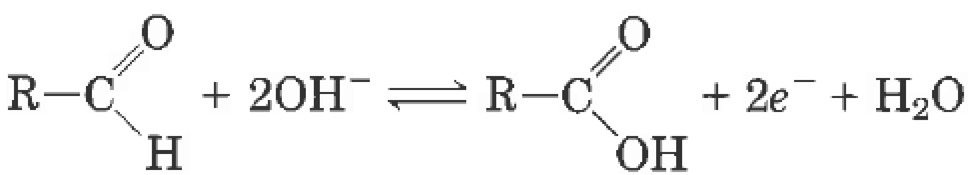
$$Fe^{2+} + Cu^{2+} \rightleftharpoons Fe^{3+} + Cu^{+}$$

can be described in terms of two half-reactions:

(1) $$Fe^{2+} \rightleftharpoons Fe^{3+} + e^{-}$$

(2) $$Cu^{2+} + e^{-} \rightleftharpoons Cu^{+}$$



(1) 

(2) $$2Cu^{2+} + 2e^{-} + 2OH^{-} \rightleftharpoons Cu_2O + H_2O$$

Reduction potentials measure affinity for electron

$A^{n+} + ne \leftrightarrow A$

$B^{n+} + ne \leftrightarrow B$

$NAD^+ + 2H^+ + 2e \leftrightarrow NADH + H^+$

$FAD + 2H^+ + 2e \leftrightarrow FADH_2$

$\frac{1}{2} O_2 + 2H^+ + 2e \leftrightarrow H_2O$

Apparatus used to measure the **standard reduction potential** of a redox pair

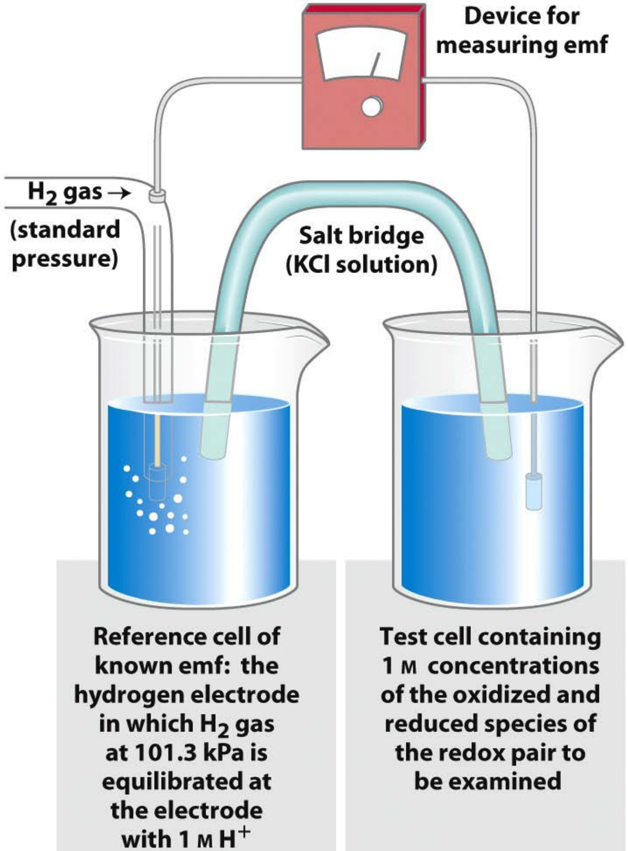
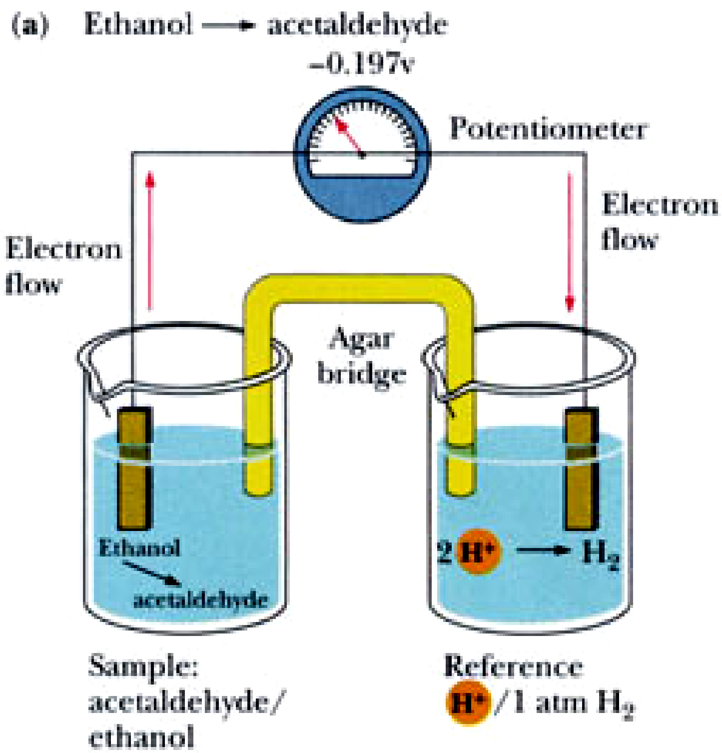
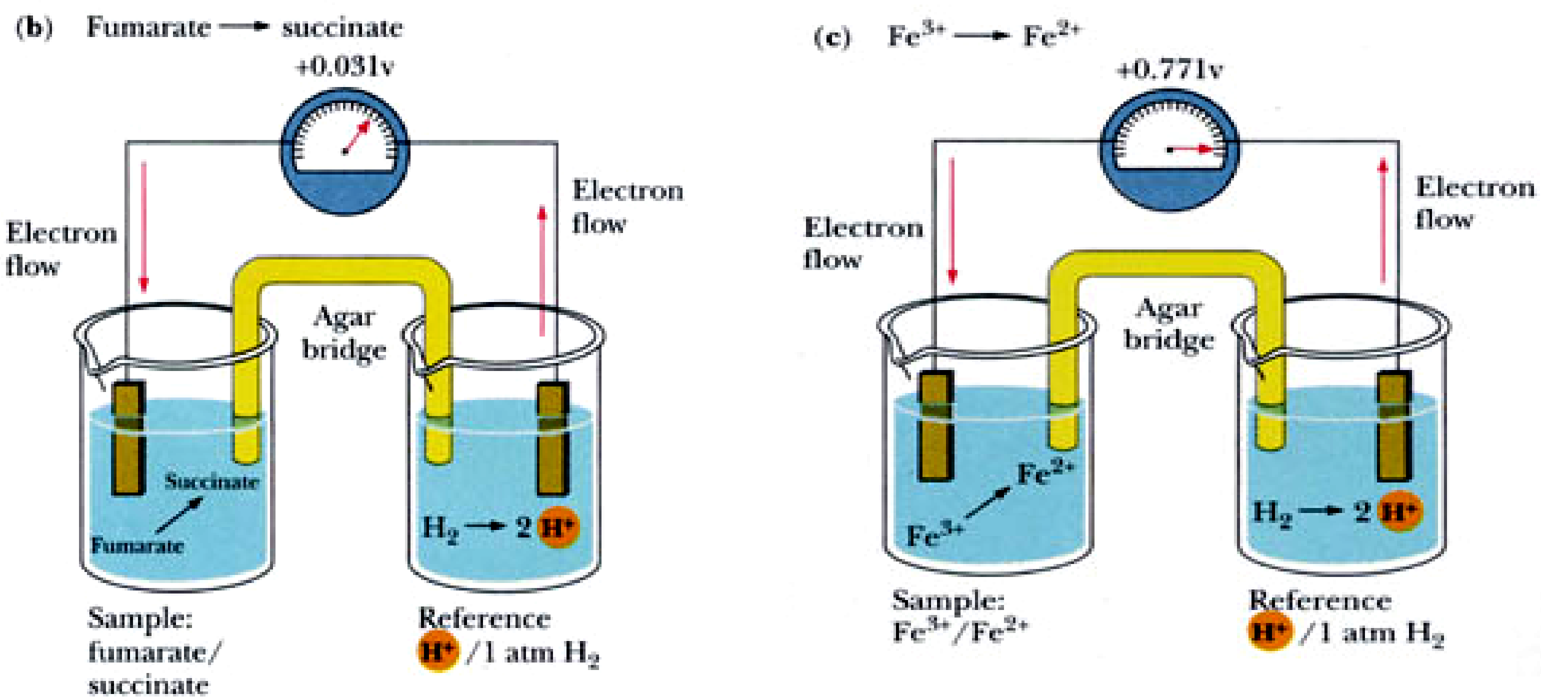


Figure 13-23



Redox couple, Sample half-cell, Reference half-cell



(b) Fumarate → succinate
+0.031v
Electron flow
Electron flow
Agar bridge
Succinate
Fumarate
$H_2 \rightarrow 2\ H^+$
Sample: fumarate/ succinate
Reference H^+ /1 atm H_2
(c) $Fe^{3+} \rightarrow Fe^{2+}$
+0.771v
Electron flow
Electron flow
Agar bridge
Fe^{2+}
Fe^{3+}
$H_2 \rightarrow 2\ H^+$
Sample: Fe^{3+}/Fe^{2+}
Reference H^+ /1 atm H_2

E^0 298K, 1M ; E'^{o} 298K, 1M , pH 7

How to calculate actual reduction potential ? p515

<u>Significance</u> of standard reduction potential:

- Values of E'^{o} can be used to predict the direction of redox reactions.
- Values can be used to analyze energy changes of redox reactions.

$\Delta G = -n\mathcal{F}\Delta E$ $\Delta G'^{o} = -n\mathcal{F}\Delta E'^{o}$

$\Delta E'^{o}$: the difference in reduction potentials between the donor and acceptor

$\Delta E'^{o} = E'^{o}$ **acceptor** – E'^{o} **donor** volts

F: Faraday's constant 96.485 J/V·mol

n: the number of electrons transferred

TABLE 13–7 Standard Reduction Potentials of Some Biologically Important Half-Reactions

Half-reaction	E'° (V)
$\frac{1}{2}O_2 + 2H^+ + 2e^- \longrightarrow H_2O$	0.816
$Fe^{3+} + e^- \longrightarrow Fe^{2+}$	0.771
$NO_3^- + 2H^+ + 2e^- \longrightarrow NO_2^- + H_2O$	0.421
Cytochrome *f* (Fe^{3+}) + $e^- \longrightarrow$ cytochrome *f* (Fe^{2+})	0.365
$Fe(CN)_6^{3-}$ (ferricyanide) + $e^- \longrightarrow Fe(CN)_6^{4-}$	0.36
Cytochrome a_3 (Fe^{3+}) + $e^- \longrightarrow$ cytochrome a_3 (Fe^{2+})	0.35
$O_2 + 2H^+ + 2e^- \longrightarrow H_2O_2$	0.295
Cytochrome *a* (Fe^{3+}) + $e^- \longrightarrow$ cytochrome *a* (Fe^{2+})	0.29
Cytochrome c (Fe^{3+}) + $e^- \longrightarrow$ cytochrome *c* (Fe^{2+})	0.254
Cytochrome c_1 (Fe^{3+}) + $e^- \longrightarrow$ cytochrome c_1 (Fe^{2+})	0.22
Cytochrome *b* (Fe^{3+}) + $e^- \longrightarrow$ cytochrome *b* (Fe^{2+})	0.077
Ubiquinone + $2H^+ + 2e^- \longrightarrow$ ubiquinol + H_2	0.045
Fumarate^{2-} + $2H^+ + 2e^- \longrightarrow$ succinate^{2-}	0.031
$2H^+ + 2e^- \longrightarrow H_2$ (at standard conditions, pH 0)	0.000
Crotonyl-CoA + $2H^+ + 2e^- \longrightarrow$ butyryl-CoA	−0.015
Oxaloacetate^{2-} + $2H^+ + 2e^- \longrightarrow$ malate^{2-}	−0.166
Pyruvate$^-$ + $2H^+ + 2e^- \longrightarrow$ lactate$^-$	−0.185
Acetaldehyde + $2H^+ + 2e^- \longrightarrow$ ethanol	−0.197
FAD + $2H^+ + 2e^- \longrightarrow FADH_2$	−0.219*
Glutathione + $2H^+ + 2e^- \longrightarrow$ 2 reduced glutathione	−0.23
$S + 2H^+ + 2e^- \longrightarrow H_2S$	−0.243
Lipoic acid + $2H^+ + 2e^- \longrightarrow$ dihydrolipoic acid	−0.29
$NAD^+ + H^+ + 2e^- \longrightarrow$ NADH	−0.320
$NADP^+ + H^+ + 2e^- \longrightarrow$ NADPH	−0.324
Acetoacetate + $2H^+ + 2e^- \longrightarrow$ β-hydroxybutyrate	−0.346
α-Ketoglutarate + CO_2 + $2H^+ + 2e^- \longrightarrow$ isocitrate	−0.38
$2H^+ + 2e^- \longrightarrow H_2$ (at pH 7)	−0.414
Ferredoxin (Fe^{3+}) + $e^- \longrightarrow$ ferredoxin (Fe^{2+})	−0.432

Source: Data mostly from Loach, R.A. (1976) In *Handbook of Biochemistry and Molecular Biology*, 3rd edn (Fasman, G.D., ed.), *Physical and Chemical Data*, Vol. 1, pp. 122–130, CRC Press, Boca Raton, FL.

* This is the value for free FAD; FAD bound to a specific flavoprotein (e.g., succinate dehydrogenase) has a different E'° that depends on its protein environment.

Table 13-7

Lehninger Principles of Biochemistry, Fifth Edition

Nutrition

Macronutrients: protein, carbohydrate, lipid

Micronutrients: vitamins, minerals

Protein

Dietary protein:

Essential amino acids: the amino acids that cannot be synthesized by higher organisms and can be obtained only in the diet.

glucogenic amino acids----glucose

ketogenic amino acids----fatty acids and keto acid

Organism's own protein:

- nitrogen positive balance
- nitrogen negative balance

Carbohydrate

The principal purpose of carbohydrate is to produce the metabolic energy, and they are also the essential components of nucleic acids, glycoproteins and glycolipids.

Lipid

Fatty acid and triacylglycerols are fuel, and phospholipids are essential components of biological membranes.

Essential fatty acids: linoleic acid (亚油酸), linolenic acid (亚麻酸), arachidonic acid (花生四烯酸)

Fiber

Vitamins

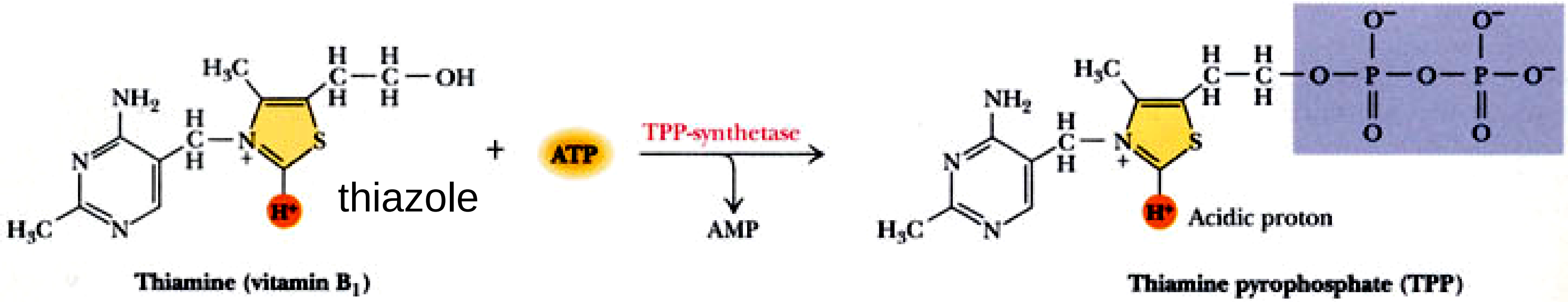
water-soluble vitamins

components or precursors of coenzymes and prosthetic group

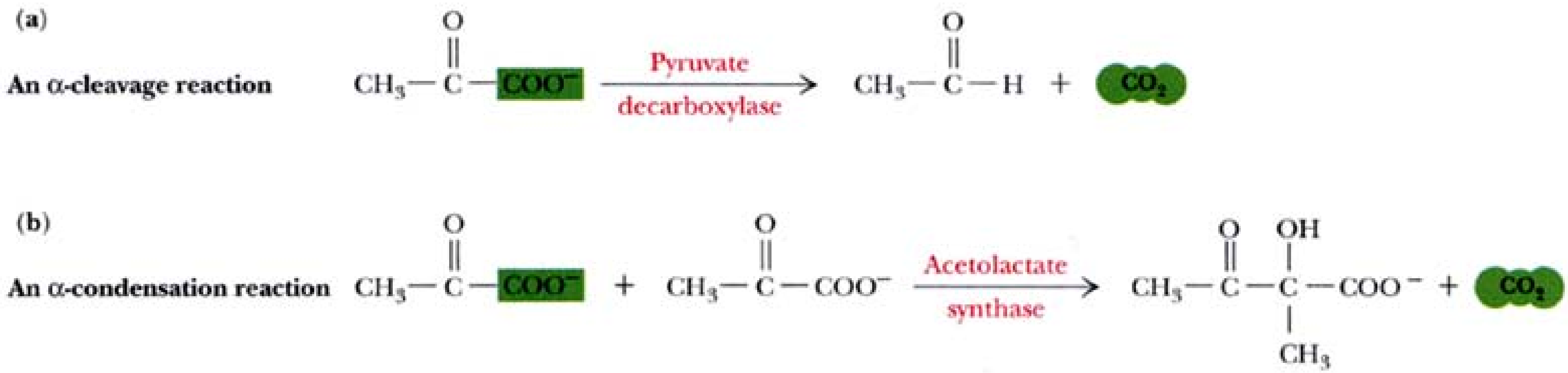
fat-soluble vitamins

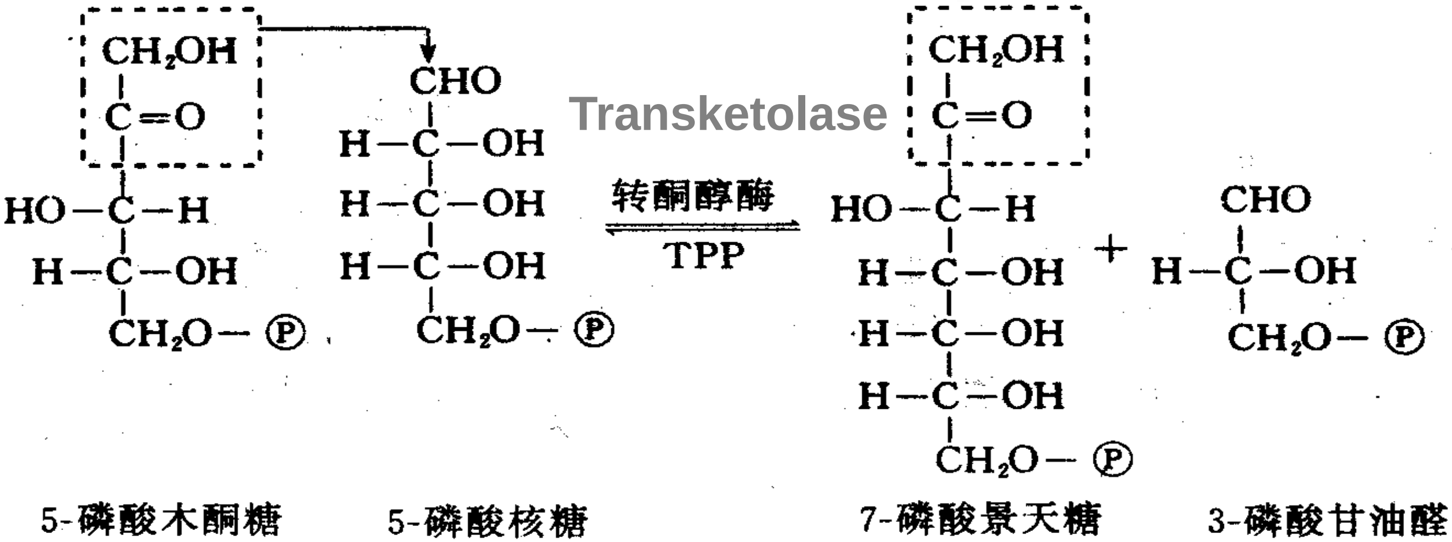
Vitamin B_1: thiamine

coenzyme： thiamine pyrophospate (硫胺素焦磷酸)



1. To participate the decarboxylation of α-keto acids;
2. To participate the formation and cleavage of α-hydroxyketones;
3. To participate the α-ketol transfer reaction.



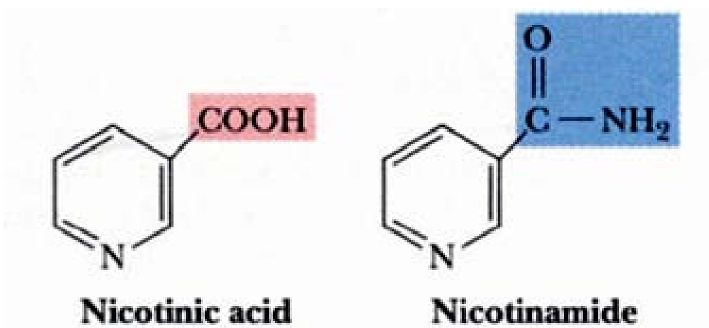


Beriberi, Neuritis   Vitamin vital amine coined by Casimir Funk

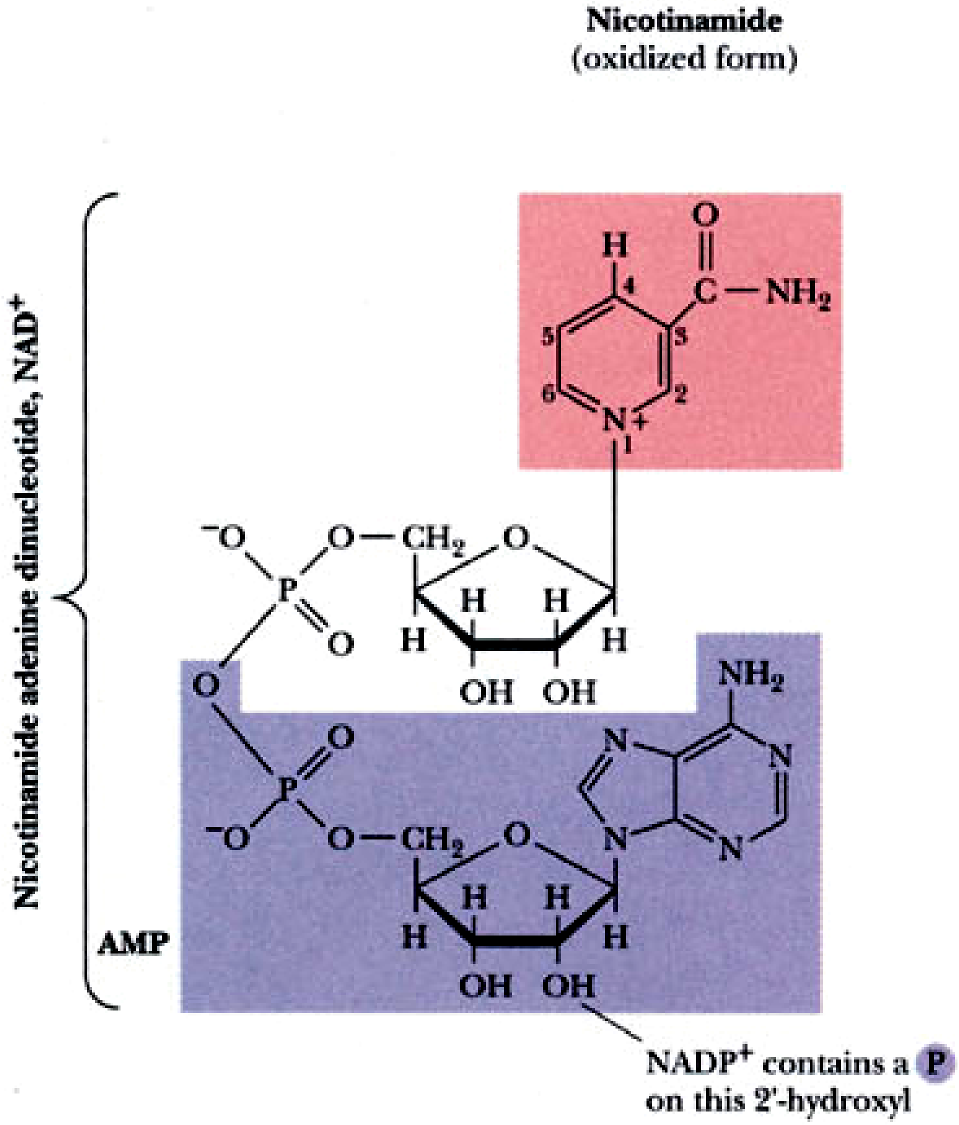
1892, **Christiaan Eijkman** found that thiamine was the anti-beriberi substance
1929, He was awarded the Nobel Prize in Physiology or Medicine

Vitamins, coenzymes of which Contain Adenine Nucleotides

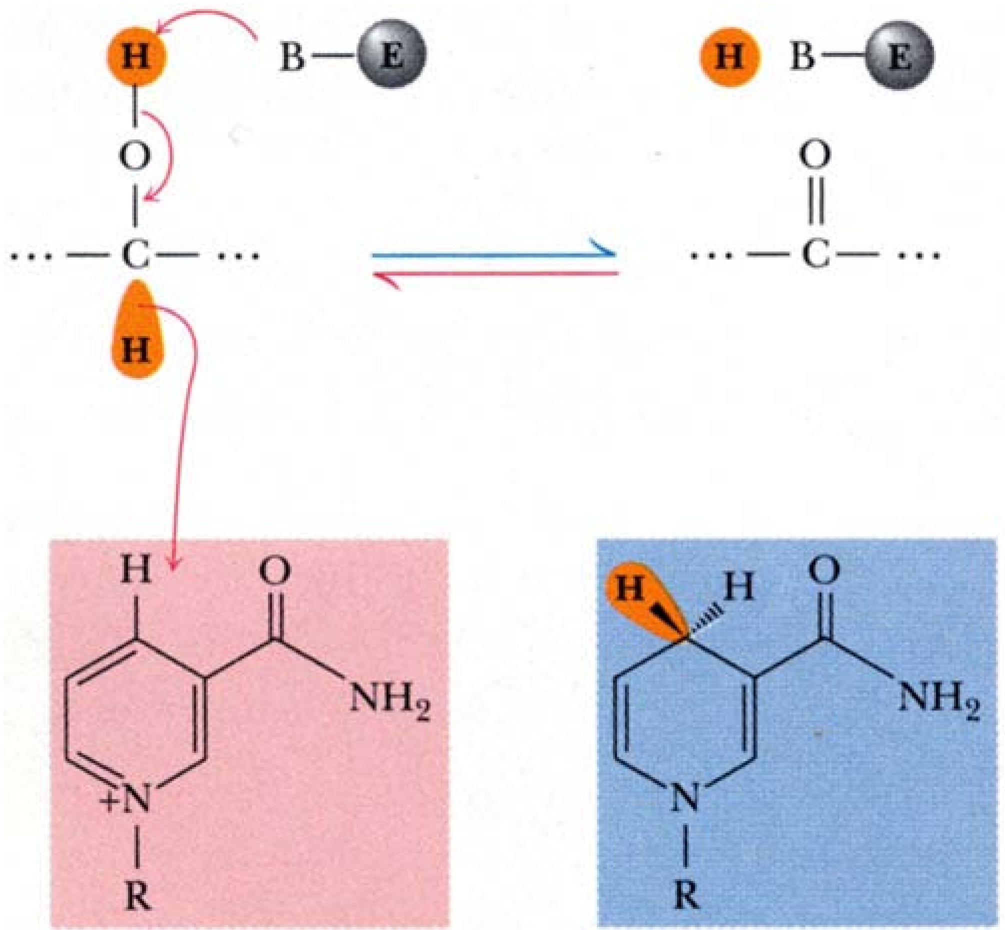
Nicotinic acid and nicotinamide
Vitamin PP



尼克酸　　尼克酰胺



coenzymes { NAD^+, $NADP^+$ }



Oxidized coenzyme
(NAD^+ or $NADP^+$)

Reduced coenzyme
(NADH or NADPH)

NAD^+ and $NADP^+$ participate the two-electron transfer reaction.

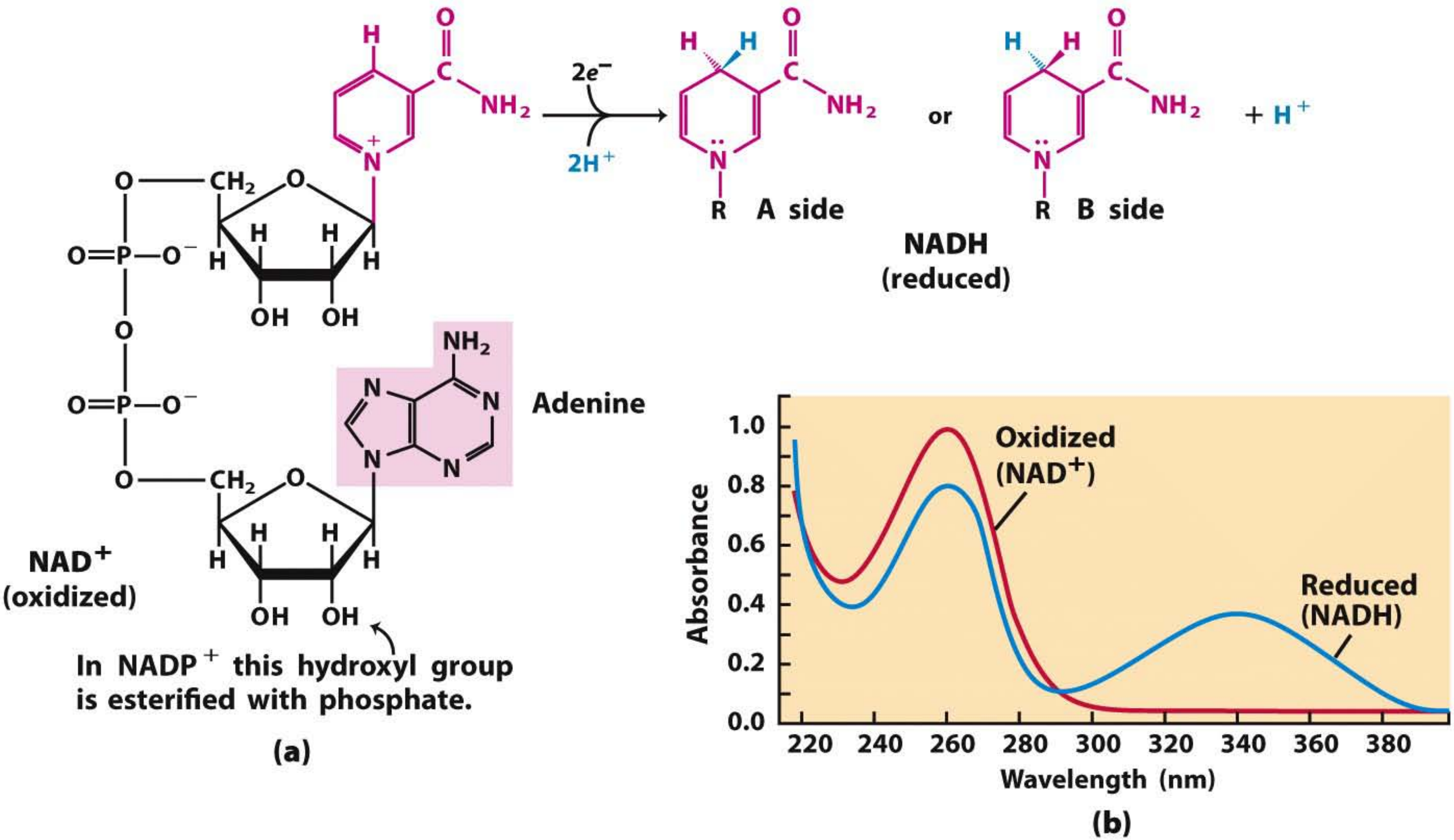


Figure 13-24
Lehninger Principles of Biochemistry, Fifth Edition

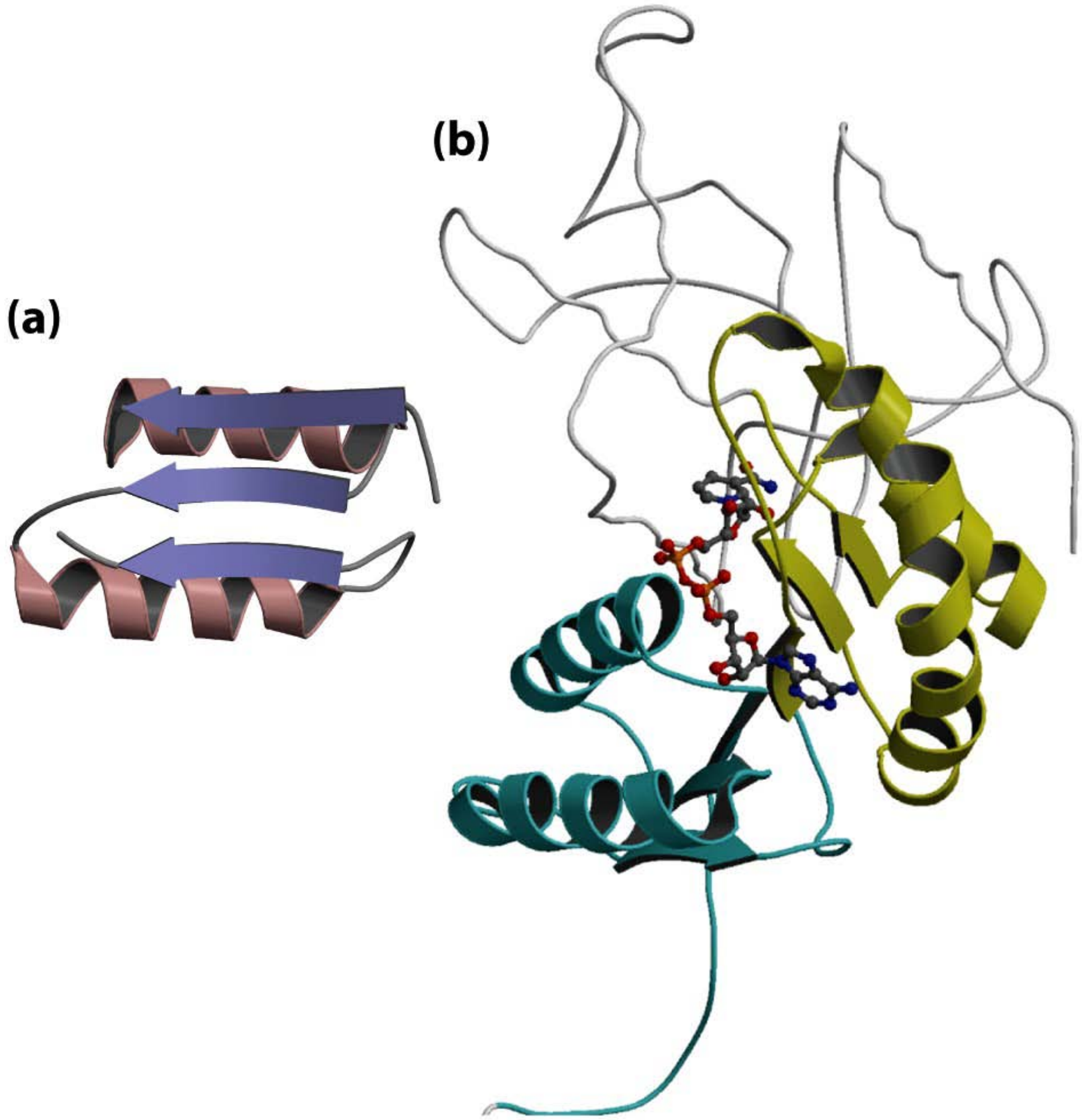
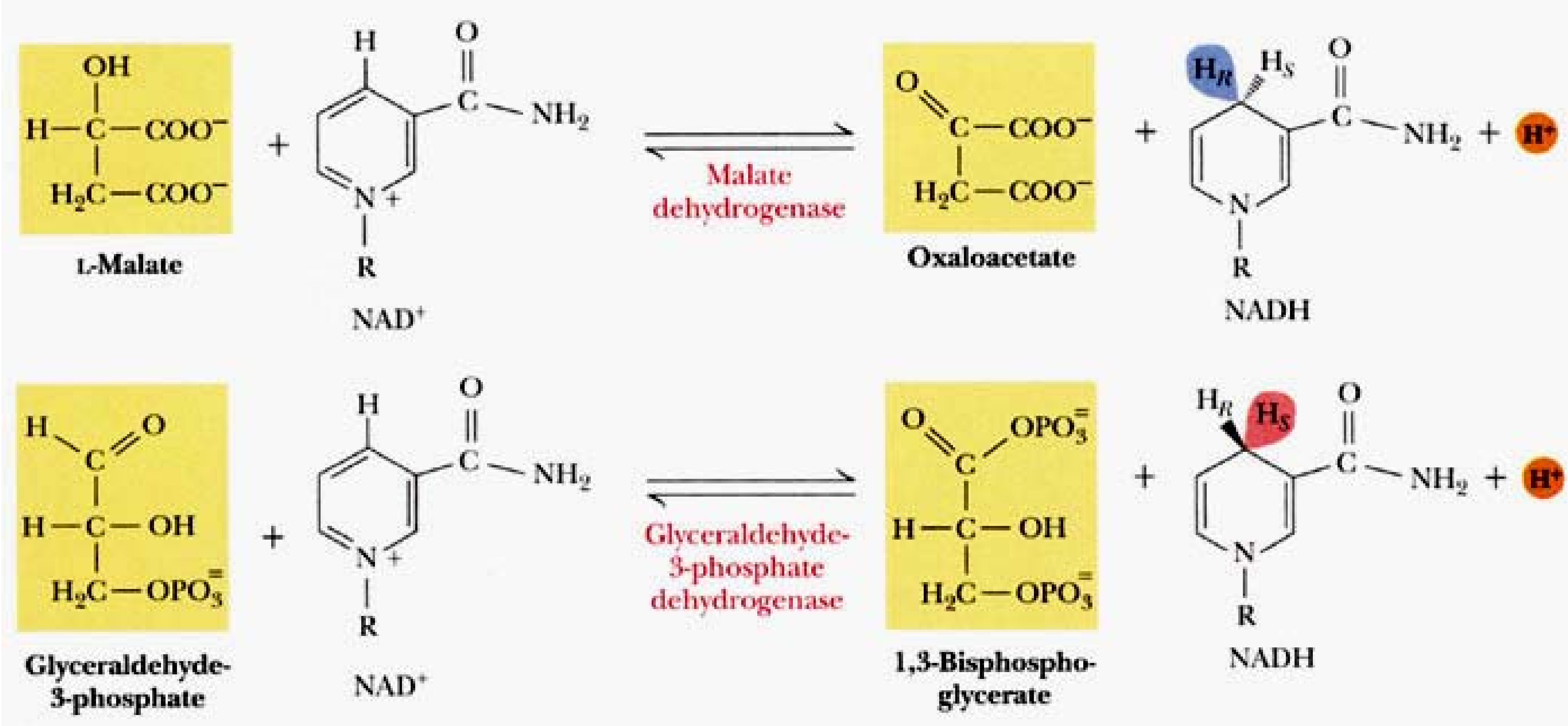
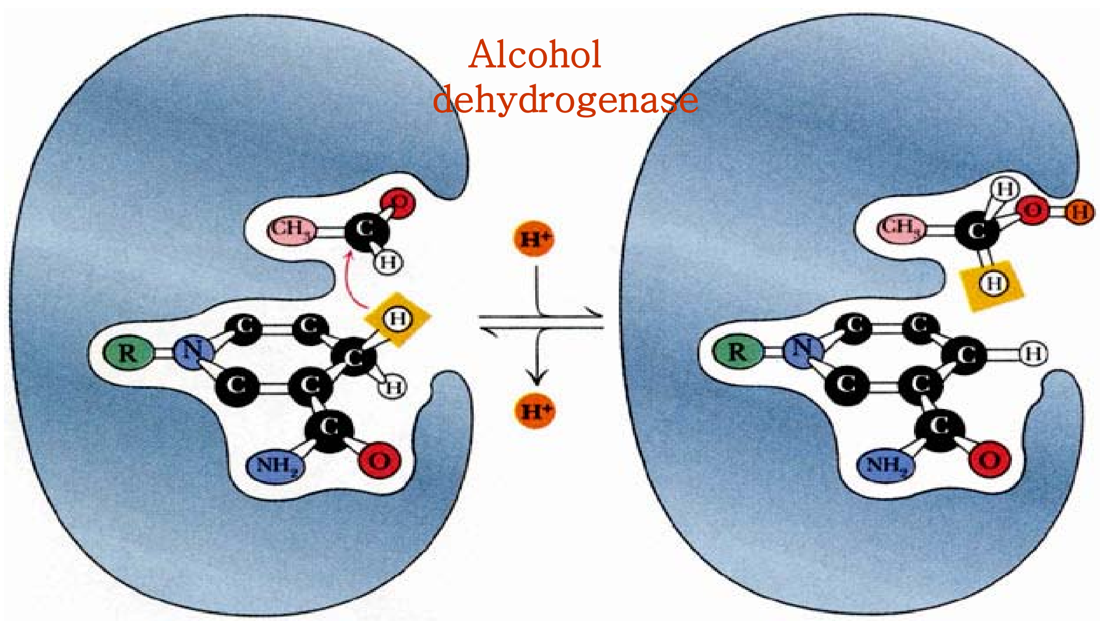


Figure 13-25
Lehninger Principles of Biochemistry, Fifth Edition





A, pro-R; B, pro-S

The asymmetric nature of the active site in dehydrogenases.

TABLE 13–8 **Stereospecificity of Dehydrogenases That Employ NAD^+ or $NADP^+$ as Coenzymes**

Enzyme	Coenzyme	Stereochemical specificity for nicotinamide ring (A or B)	Text page(s)
Isocitrate dehydrogenase	NAD^+	A	624
α-Ketoglutarate dehydrogenase	NAD^+	B	625
Glucose 6-phosphate dehydrogenase	$NADP^+$	B	560
Malate dehydrogenase	NAD^+	A	628
Glutamate dehydrogenase	NAD^+ or $NADP^+$	B	680
Glyceraldehyde 3-phosphate dehydrogenase	NAD^+	B	535
Lactate dehydrogenase	NAD^+	A	547
Alcohol dehydrogenase	NAD^+	A	547

Table 13-8
Lehninger Principles of Biochemistry, Fifth Edition

A, pro-R; B, pro-S

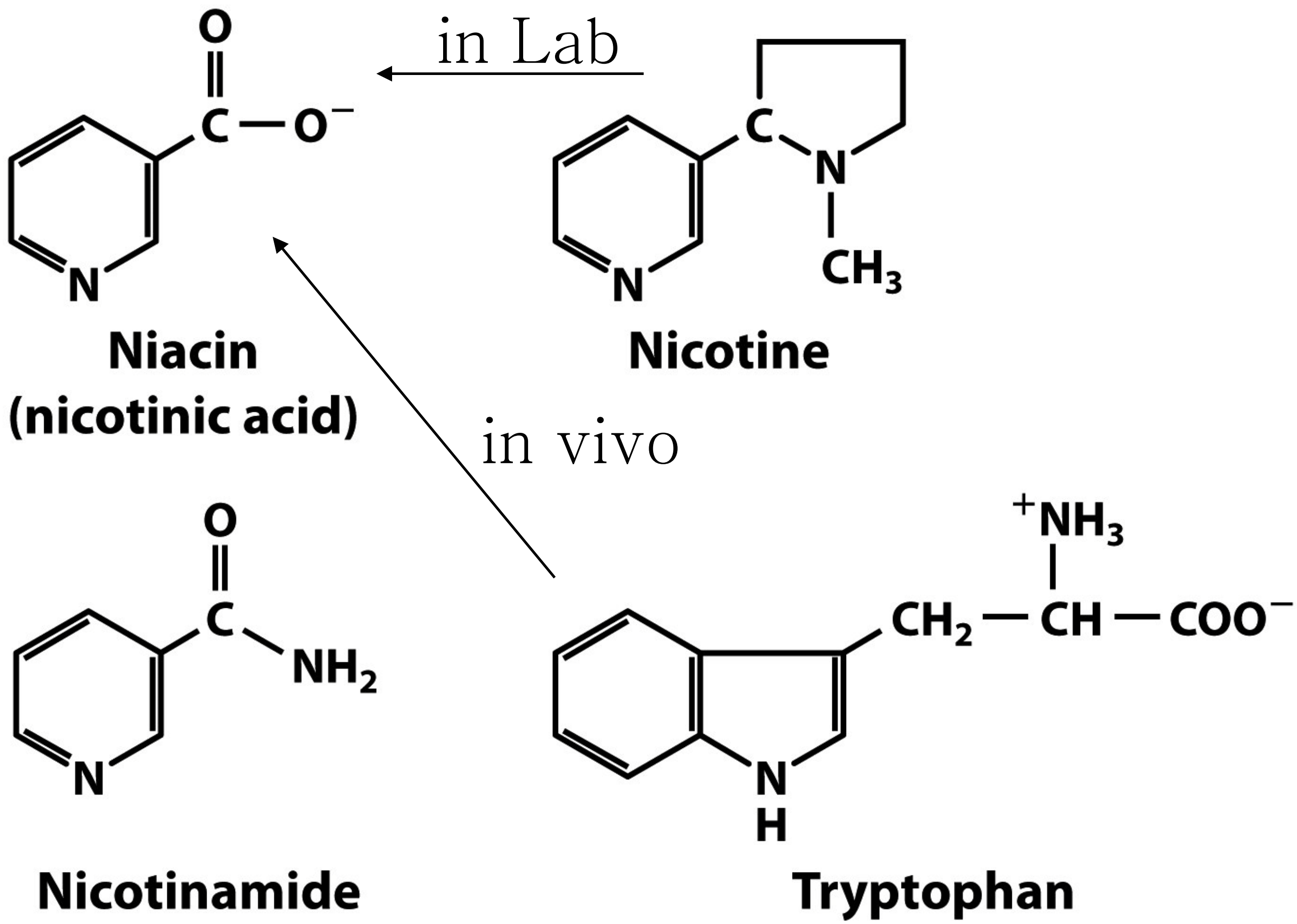


Figure 13-26
Lehninger Principles of Biochemistry, Fifth Edition

Pellagra, dermatitis, diarrhea, dementia

Frank Strong, 1908–1993

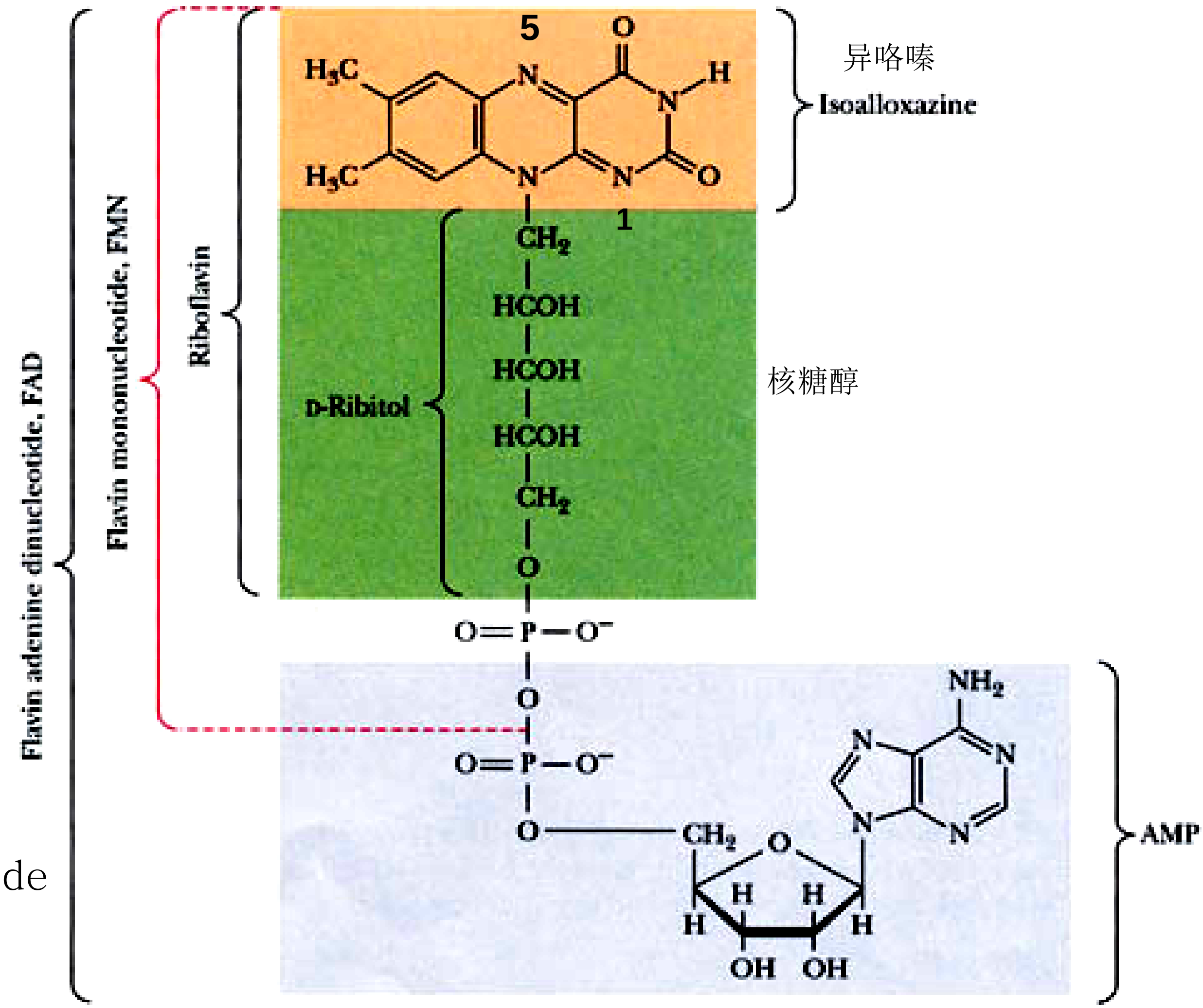
D. Wayne Woolley, 1914–1966

Conrad Elvehjem, 1901–1962

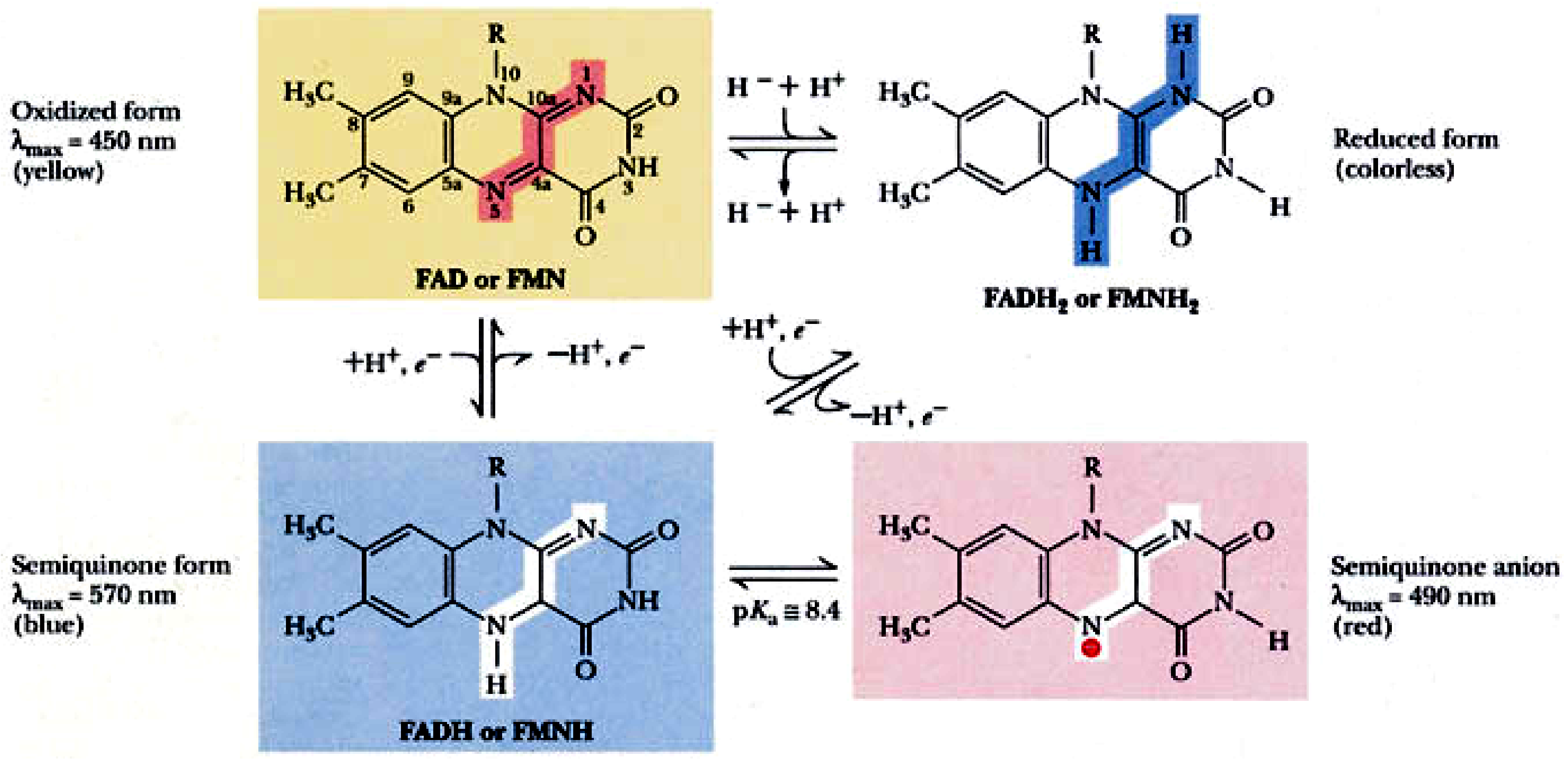
Unnumbered 13 p519
Lehninger Principles of Biochemistry, Fifth Edition

Vitamin B_2: Riboflavin （核黄素）

coenzymes: FMN, FAD



Flavin mononucleotide
Flavin adenine dinucleotide



The redox states of FAD and FMN

Flavin coenzymes participate in one or two-electron transfer reactions.

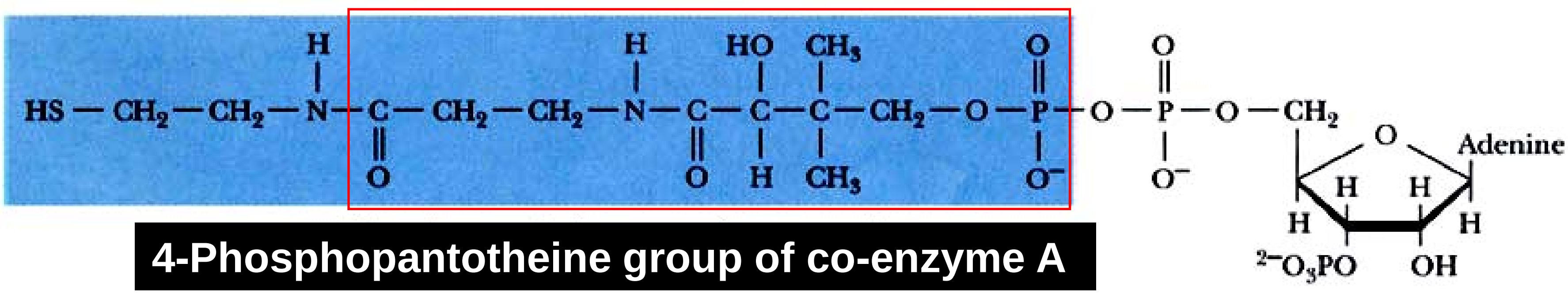
TABLE 13–9 Some Enzymes (Flavoproteins) That Employ Flavin Nucleotide Coenzymes

Enzyme	Flavin nucleotide	Text page(s)
Acyl–CoA dehydrogenase	FAD	653
Dihydrolipoyl dehydrogenase	FAD	619
Succinate dehydrogenase	FAD	628
Glycerol 3-phosphate dehydrogenase	FAD	732
Thioredoxin reductase	FAD	888
NADH dehydrogenase (Complex I)	FMN	712–714
Glycolate oxidase	FMN	787

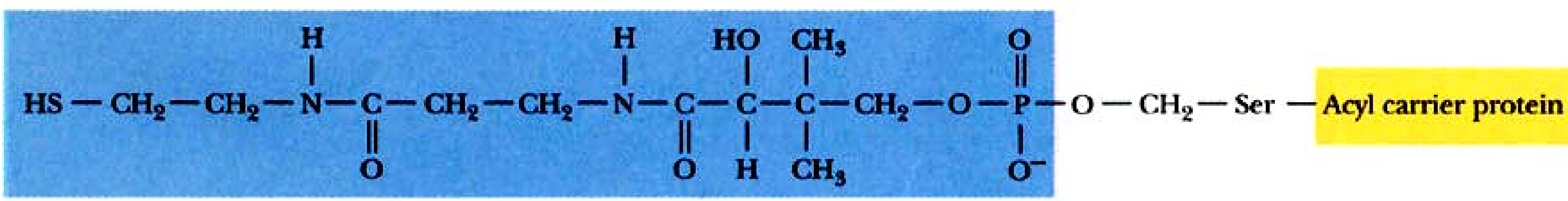
Table 13-9
Lehninger Principles of Biochemistry, Fifth Edition

Vitamin B_3: Pantothenic acid (泛酸)

Beta-Mercaptoethylamine **Pantothenic acid** coenzyme A



4-Phosphopantotheine group of co-enzyme A



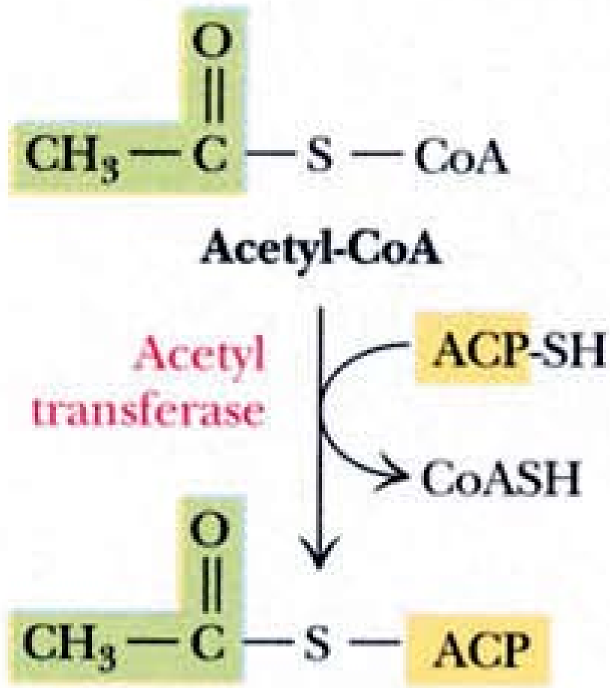
Phosphopantotheine group of ACP

The structures of coenzyme A and ACPs (acyl carrier proteins)

Fritz Lipmann received the Nobel Prize in 1953

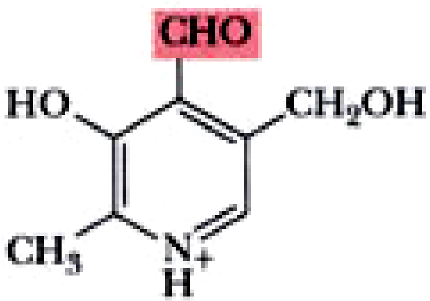
The function of coenzyme A:

Activation of acyl groups for transfer by nucleophilic attack.

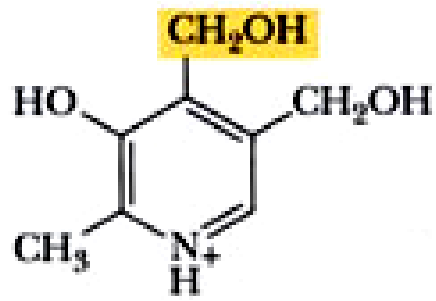


The first step in fatty acid biosynthesis.

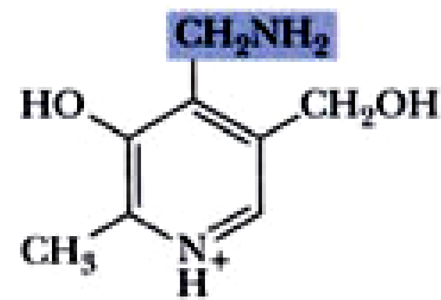
Vitamin B_6 and pyridoxal phosphate



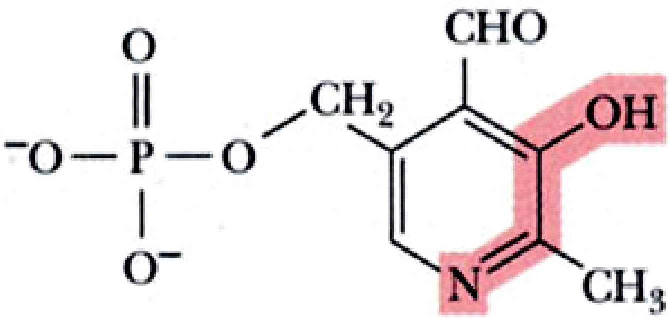
Pyridoxal



Pyridoxine or pyridoxol

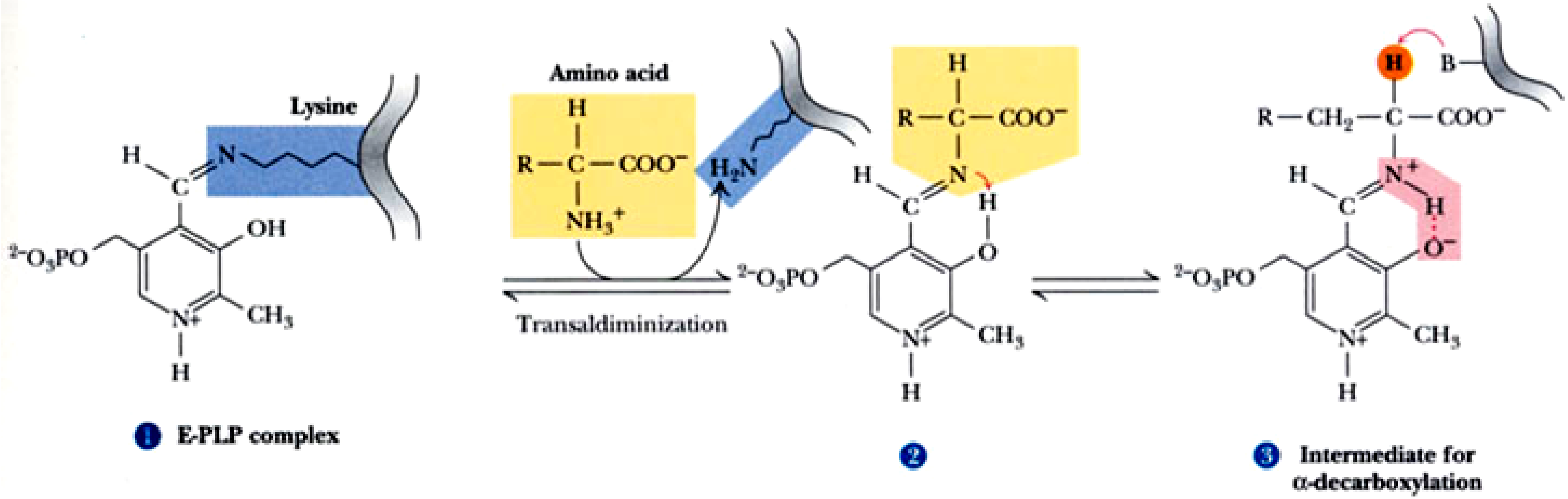


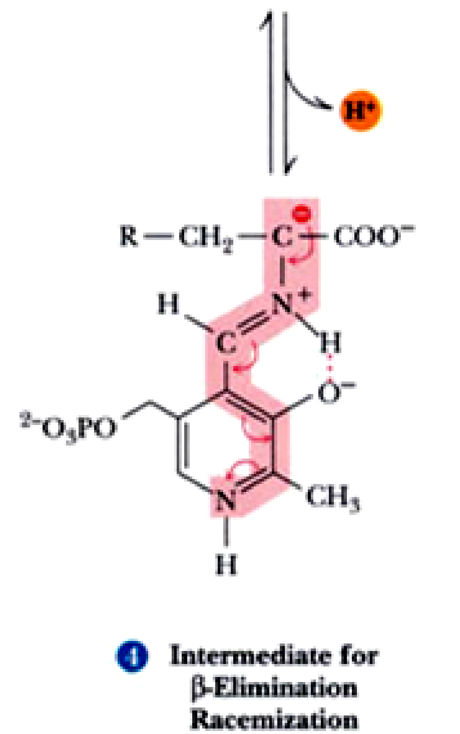
Pyridoxamine



Coenzyme Pyridoxal 5-phosphate

Function: transamination, α- and β-decarboxylation, β- and γ-eliminations, racemizations, and aldol reaction



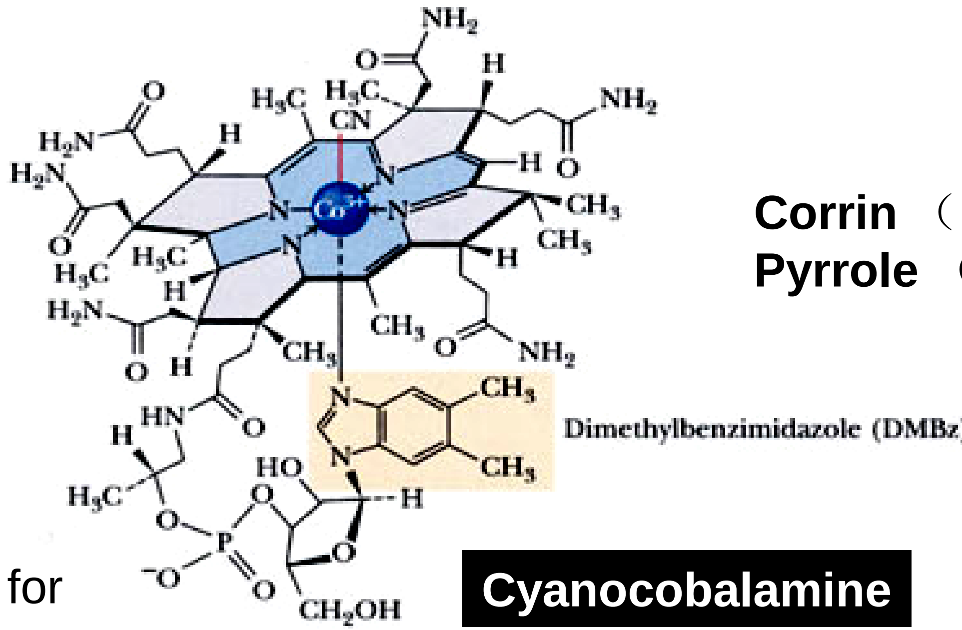


Pyridoxal-5-phosphate forms stable Schiff base adducts with amino acids.

Vitamin B_{12}: cyanocobalamin

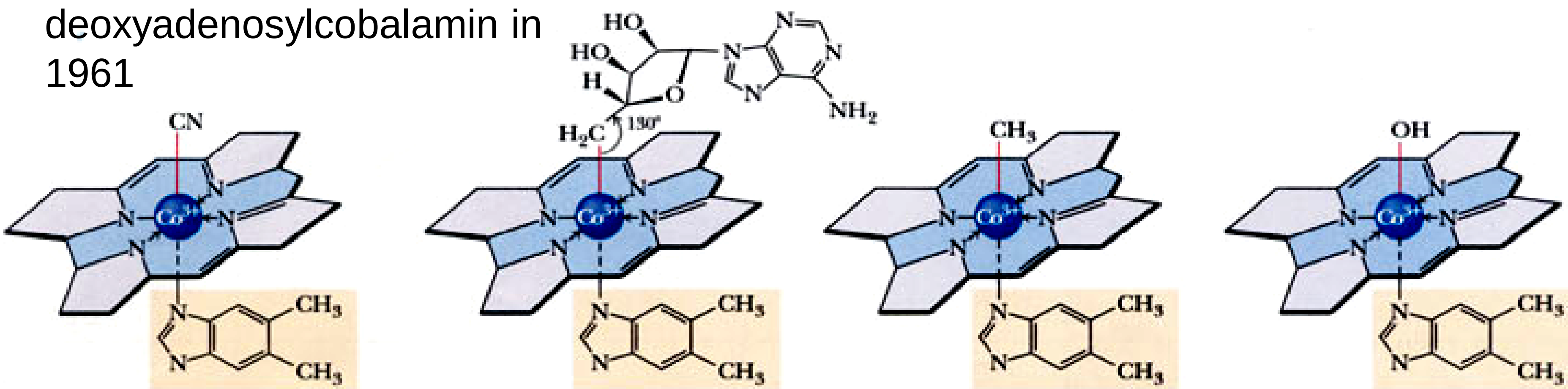
Whipple、Minot and Murphy Were awarded Nobel Prize in **1934** for their finding that pernicious anemia could be prevented by eating liver

In **1964 Hodgkin** was awarded the Nobel Prize for structural resolution of 5’-deoxyadenosylcobalamin in 1961



Corrin （咕啉）
Pyrrole （吡咯）

Cyanocobalamine



Cyanocobalamin
Vitamin B_{12}

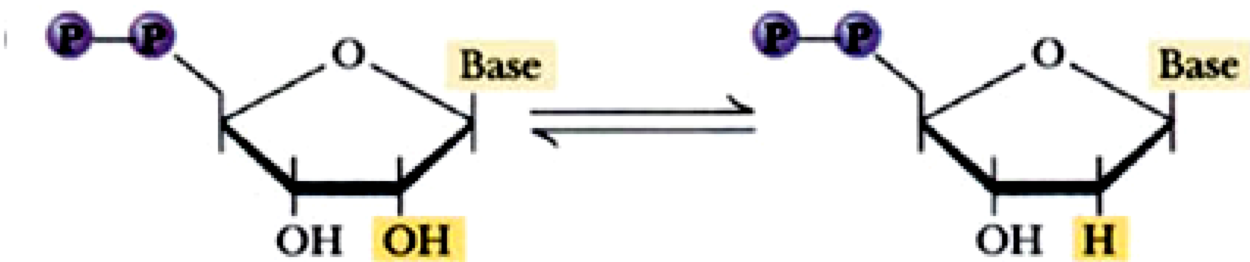
5'-Deoxyadenosylcobalamin

Methylcobalamin

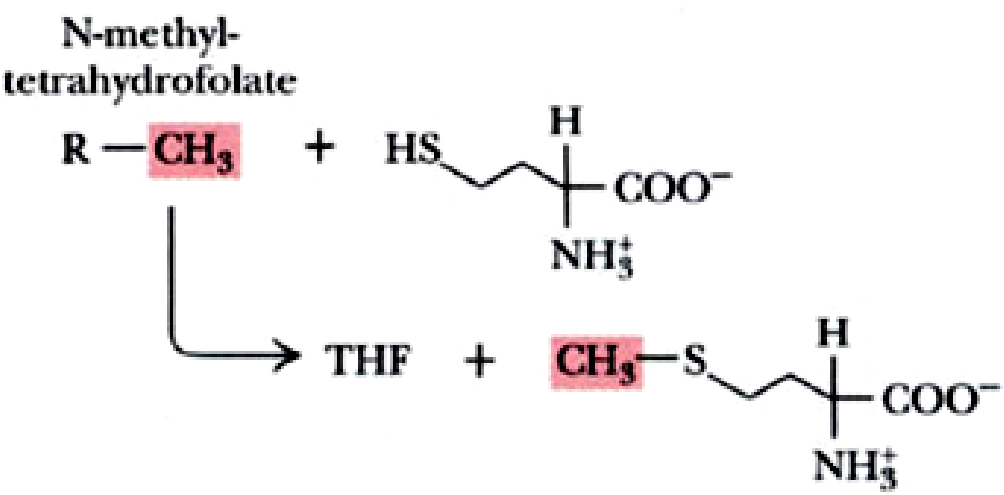
Hydroxocobalamin
Vitamin B_{12b}

Coenzyme Forms

Intramolecular rearrangements



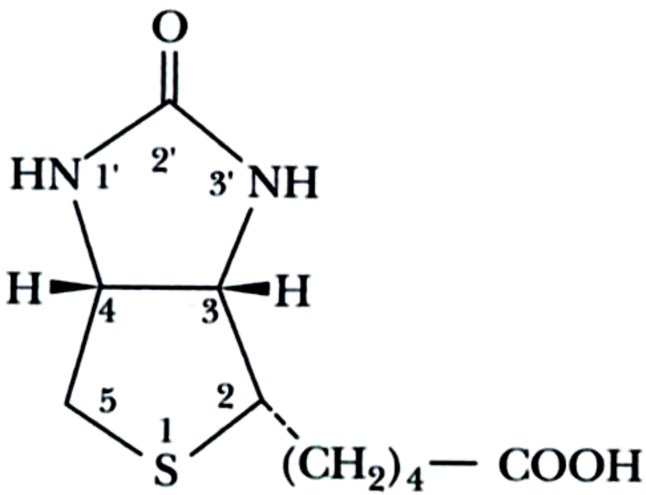
Ribonucleotide reduction



Methyl transfer in methionine synthesis

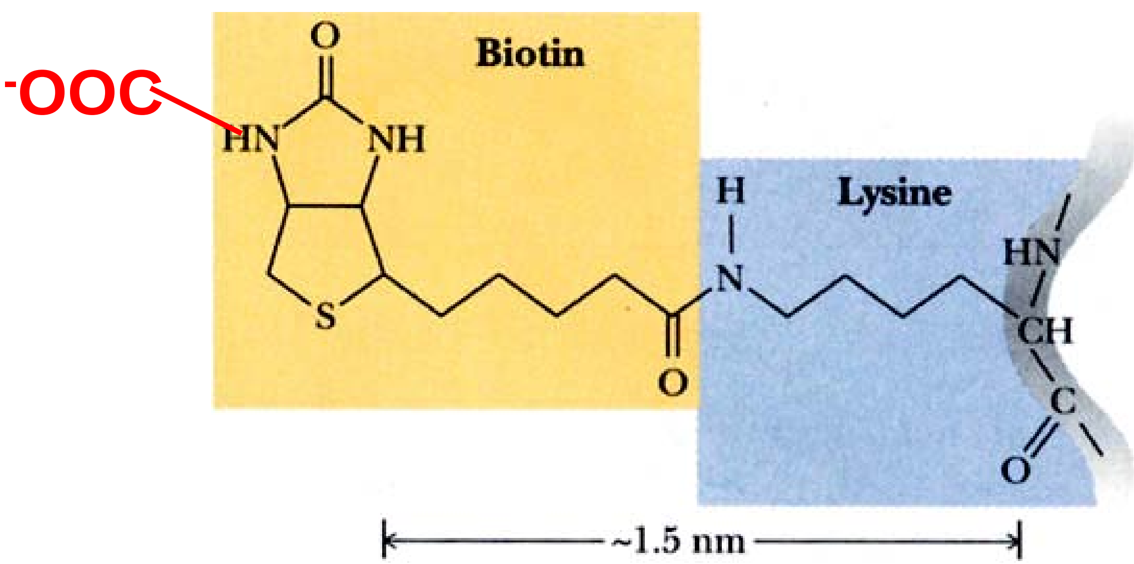
Vitamin B12 functions as a coenzyme.

Biotin （生物素）



Avidin, egg white injury

The structure of biotin



The biotin-lysine (biocytin) complex

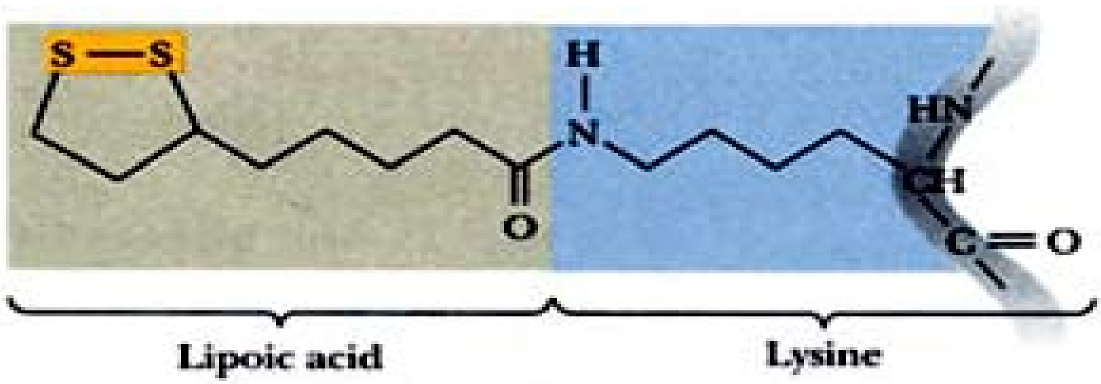
Biotin is covalently linked to a protein via the ε-NH_3 of a Lys residue.

Function: Mobile carboxyl group carrier

Lipoic acid （硫辛酸）

Lipoic acid, oxidized form

Reduced form



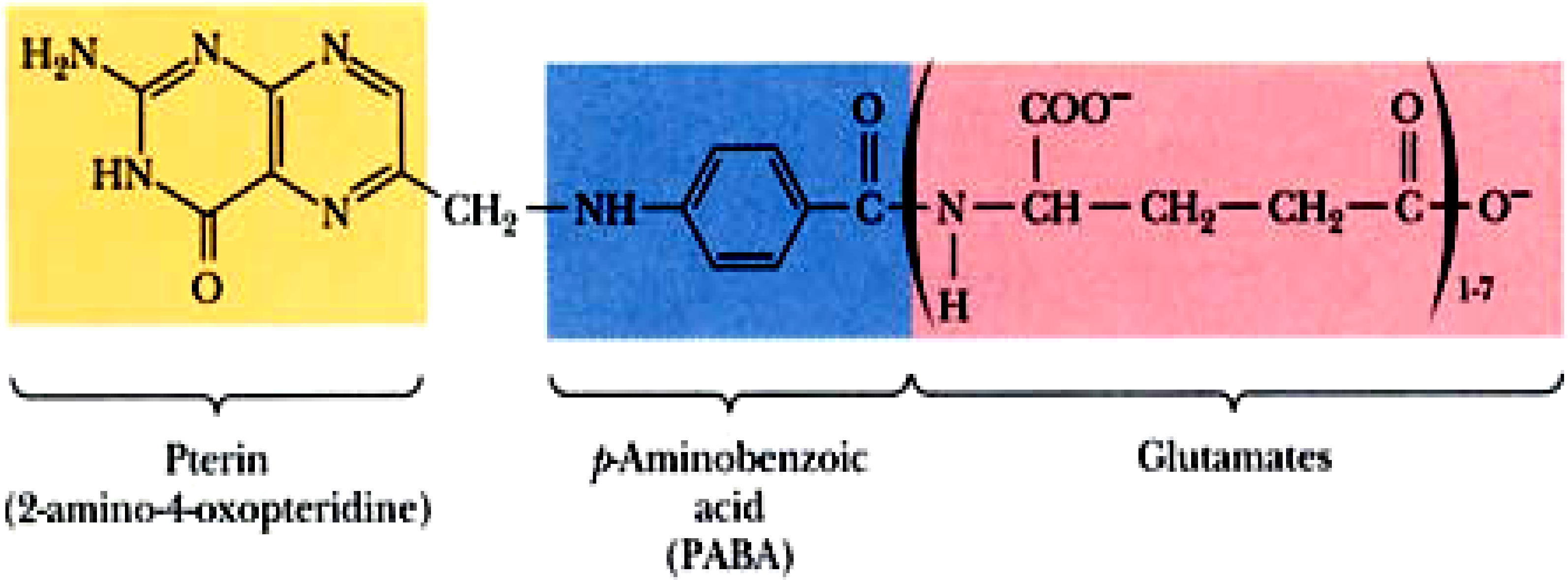
Lipoamide complex

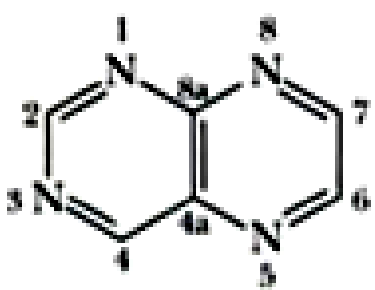
Lipoyl-lysine complexes

Lipoic acid is an acyl group carrier in pyruvate dehydrogenase and α-ketoglutarate dehydrogenase multienzyme complexes .

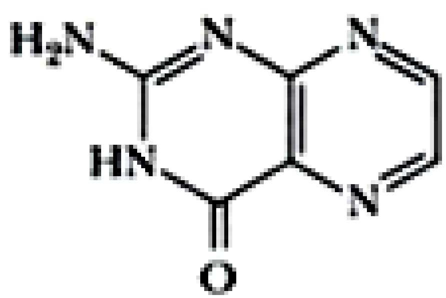
$$CH_3COCOOH + CoA + NAD^+ \xrightarrow[\text{multienzyme complexes}]{\text{pyruvate dehydrogenase}} CH_3CO\sim SCoA + CO_2 + NADH + H^+$$

Folic acid



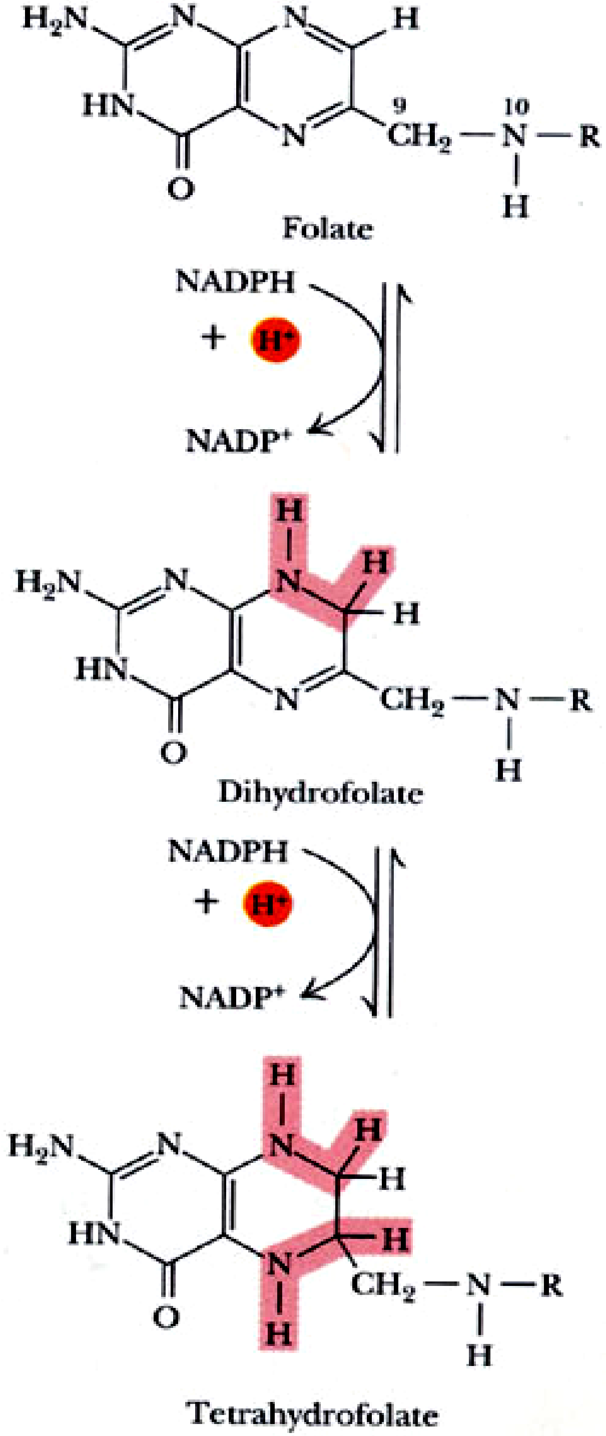


Pteridine



Pterin: 2-amino-4-oxopteridine

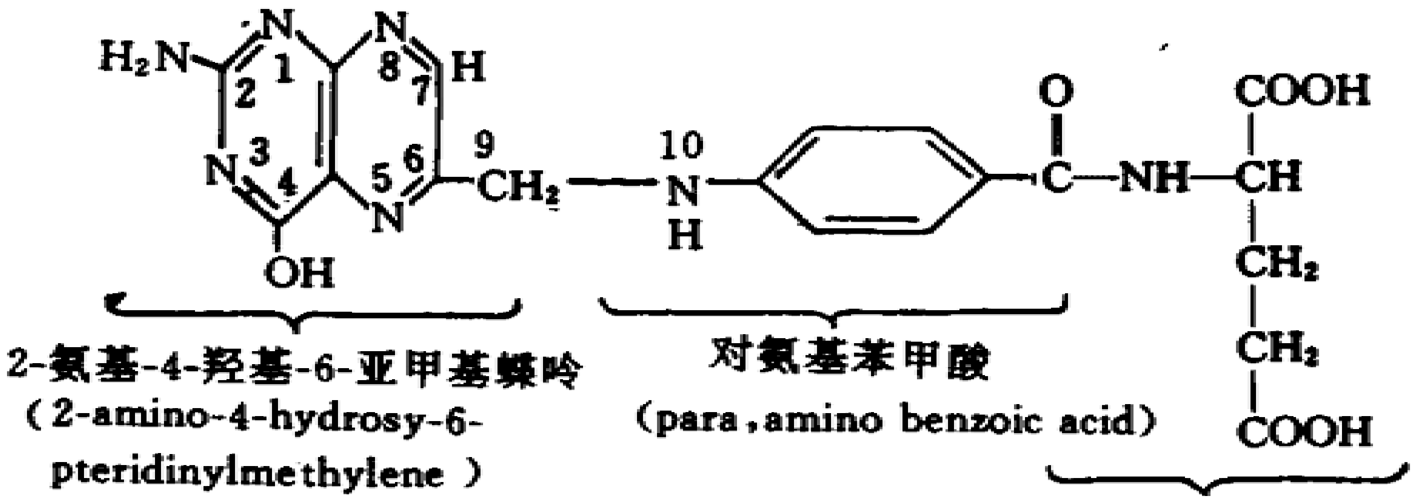
Structures of folic acid , pteridine and pterin.



Formation of tetrahydrofolate (THF) from folic acid.

Coenzyme: THF

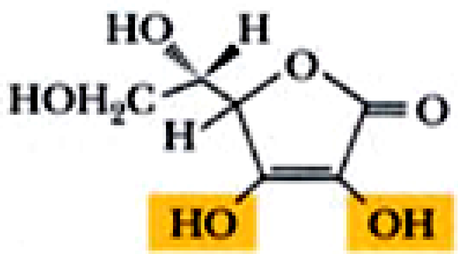
THF are acceptors and donors (carriers) of one-carbon units except CO_2. The biosynthesis for Met, purines and thymine rely on the incorporation of one-carbon units from THF.



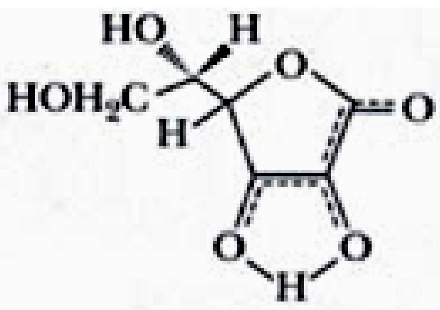
One-carbon units are bound to THF at N_5 and/or N_{10} nitrogens.

Vitamin C: ascorbic acid (抗坏血酸)
anti-scorbutic

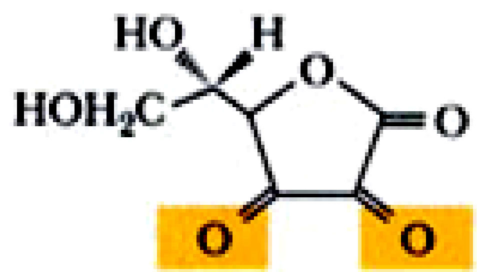
1937 Nobel Prize



Ascorbic acid (Vitamin C)



L-Ascorbate free radical

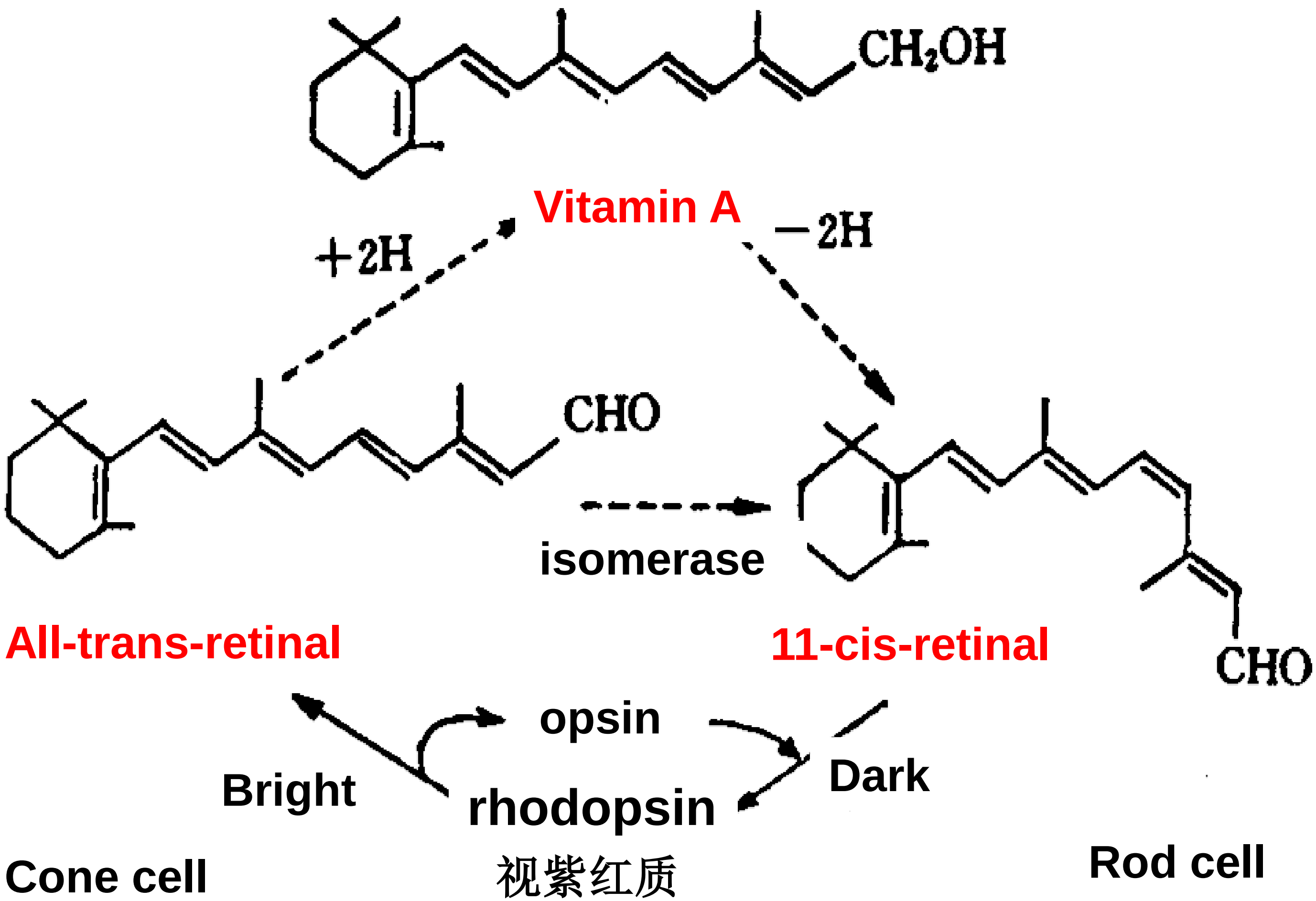


Dehydro-L-ascorbic acid

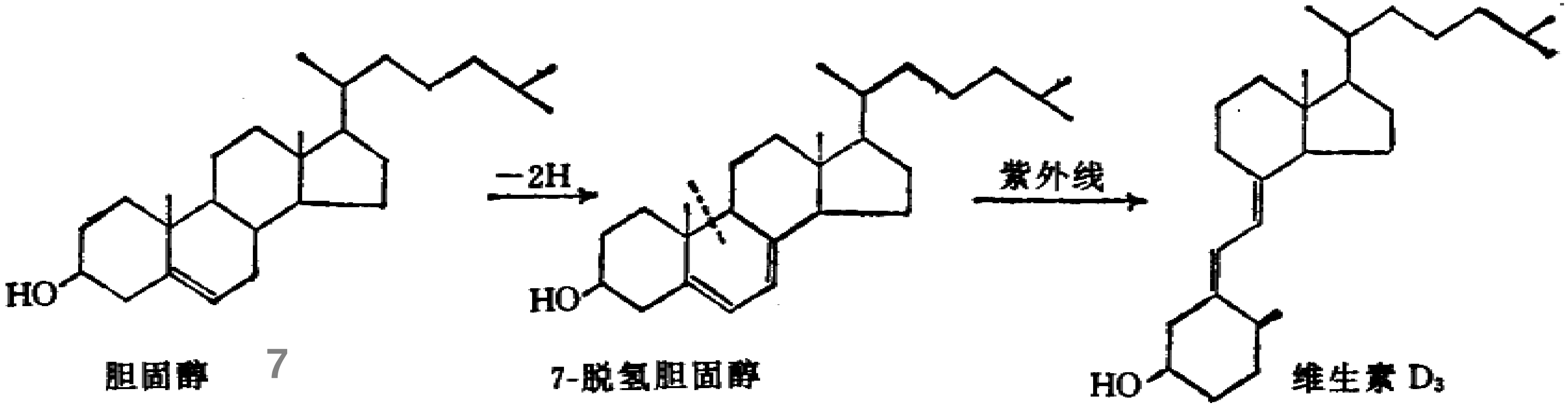
the biochemical functions for ascorbic acid :

1. it’s an important reductant.
2. it participates in hydroxylation.
3. prevents anemia, inhibits allergic responses, and stimulates the immune system

Vitamin A (retinol) 视黄醇



Vitamin D

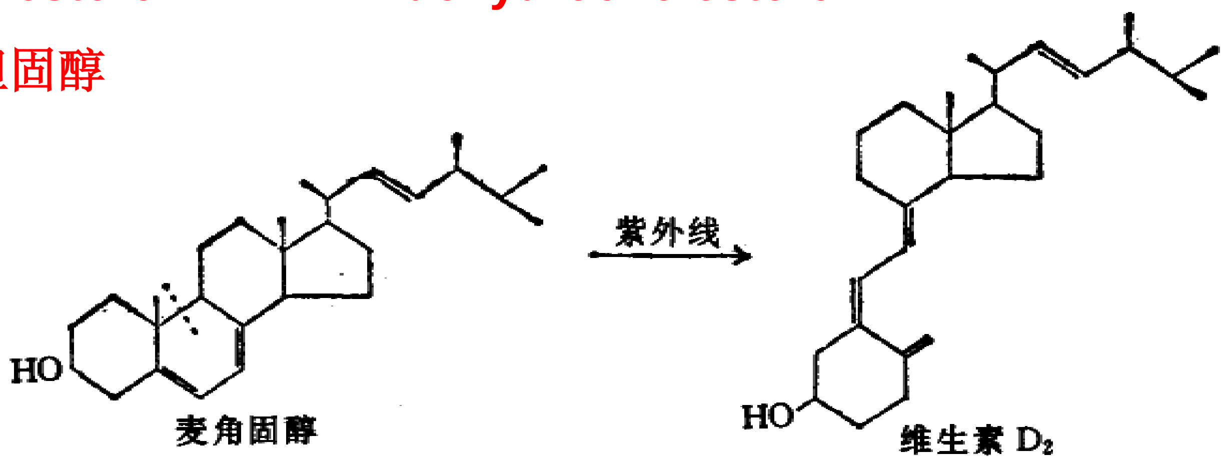


Cholesterol

7-dehydrocholesterol

Vitamin D_3

胆固醇



Ergosterol 麦角固醇

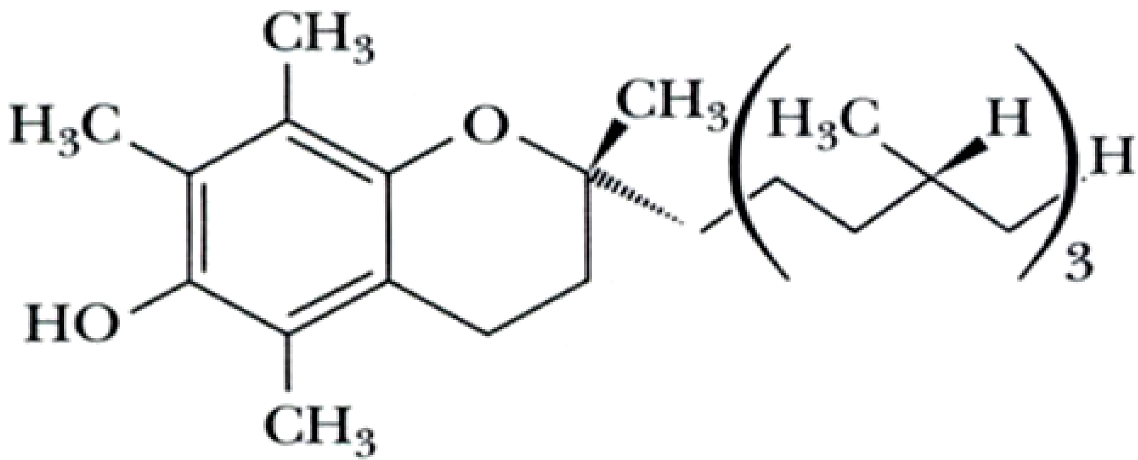
Vitamin D_2

Vitamin D3 is converted to 1,25 –dihydroxyvitamin D3 in liver and kidney

1,25 –dihydroxyvitamin D3 is the active form of vitamin D, it acts to regulate calcium and phosphate metabolism.

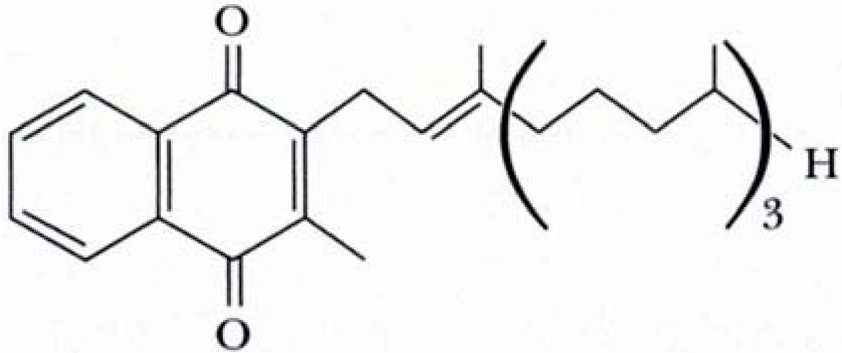
Vitamin D deficiency in children leads to rickets, and in adults osteomalacia.

Vitamin E

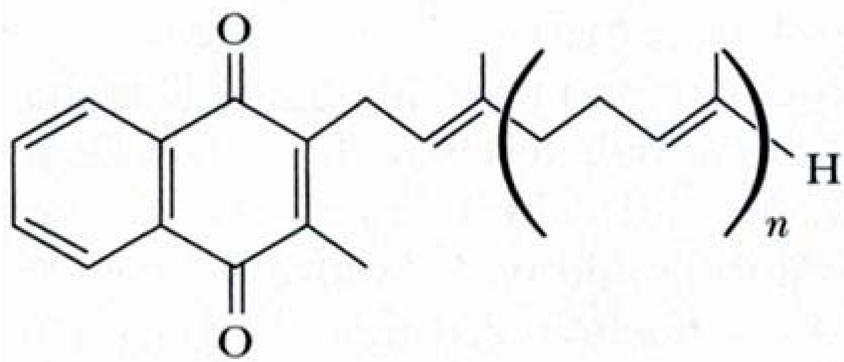


Vitamin E (α-tocopherol)

Vitamin K

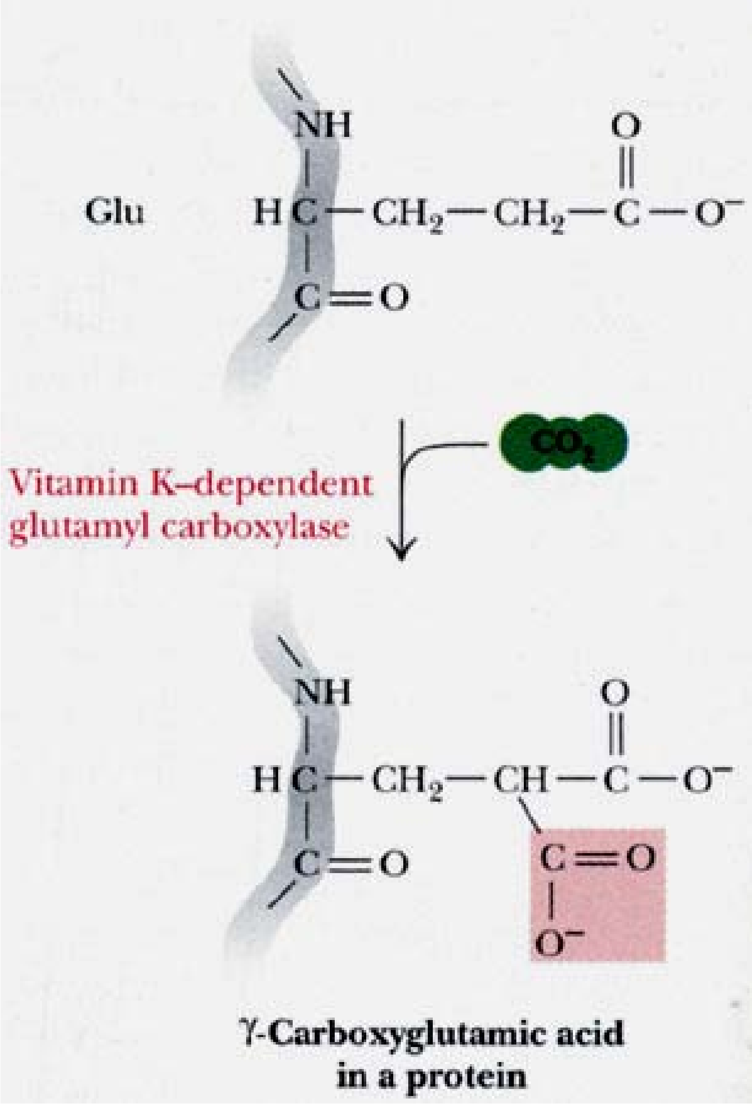


Vitamin K_1
(phylloquinone)



Vitamin K_2
(menaquinone series)

Activation of Clotting factor



→ Activation of prothrombin (II), clotting factor Ⅶ, Ⅸ and Ⅹ.