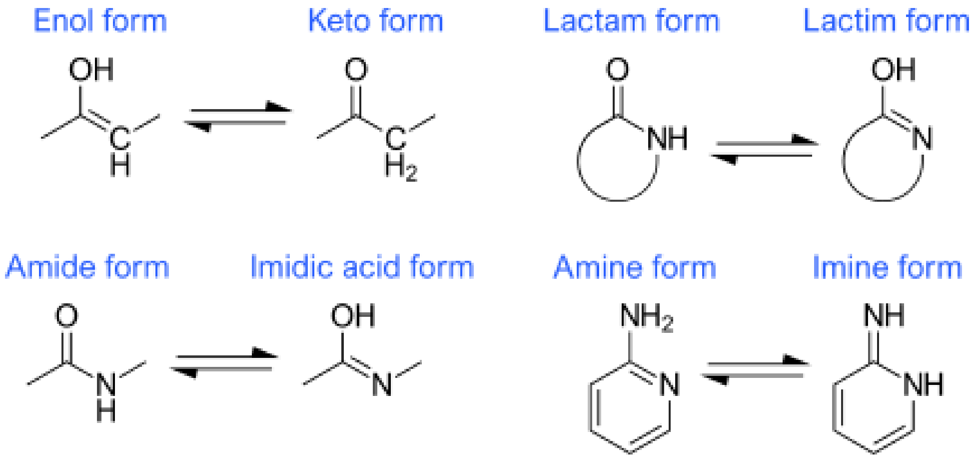
Other phosphorylated compounds and thioesters also have large free energy of hydrolysis

- Tautomerization (호변이성)
  ; Phosphoenolpyruvate

Tautomers are constitutional isomers of organic compounds that readily interconvert. This reaction commonly results in the relocation of a proton



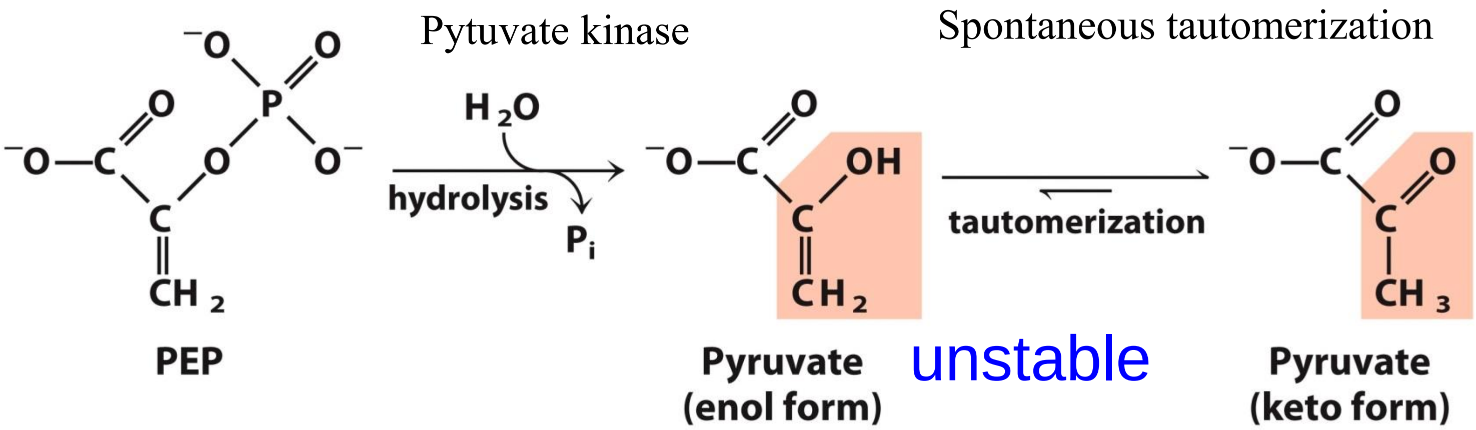
- Resonance stabilization by removing Pi
  ; 1,3-biphosphoglycerate, phosphocreatine

- Thioester

Several phosphorylated compounds have large ΔG°′ for hydrolysis

1. Hydrolysis of phosphoenolpyruvate (PEP)

- Electrostatic repulsion within the reactant molecule is relieved
- The products (P_i) are stabilized via resonance, or by more favorable solvation
- The product undergoes further tautomerization



Pytuvate kinase

Spontaneous tautomerization

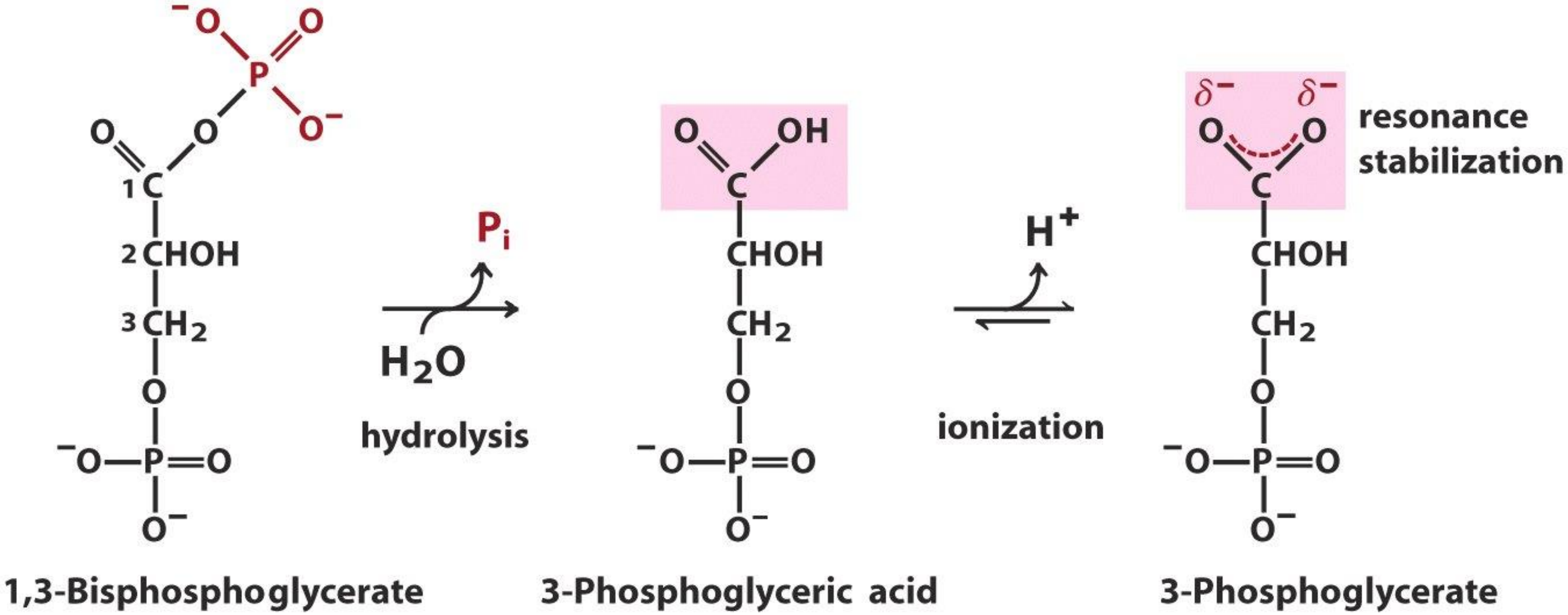
unstable

stable

$$PEP^{3-} + H_2O \longrightarrow \text{pyruvate}^{-} + HPO_4^{2-}$$

$$\Delta G'^{\circ} = -61.9 \text{ kJ/mol}$$

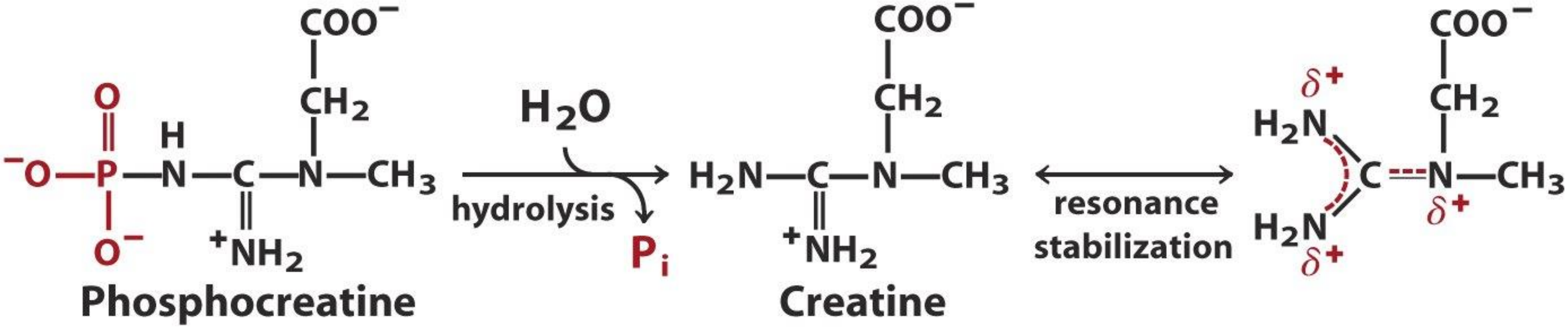
2. Hydrolysis of 1,3-bisphosphoglycerate (1, 3,BPG)



$$\text{1,3-Bisphosphoglycerate}^{4-} + H_2O \longrightarrow \text{3-phosphoglycerate}^{3-} + P_i^{2-} + H^+$$

$$\Delta G'^{\circ} = -49.3 \text{ kJ/mol}$$

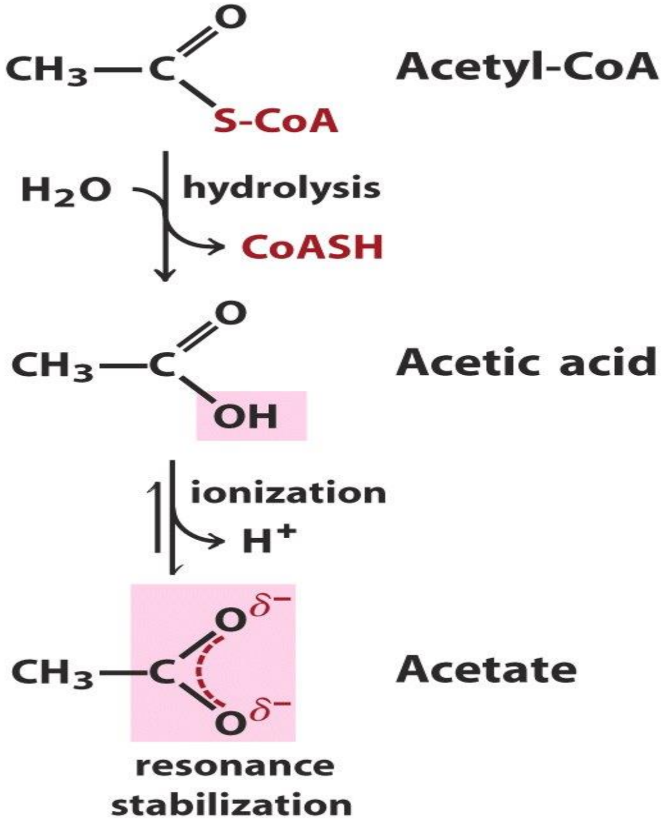
3. Hydrolysis of phosphocreatine



$$\text{Phosphocreatine}^{2-} + H_2O \longrightarrow \text{creatine} + P_i^{2-}$$

$$\Delta G'^{\circ} = -43.0\ \text{kJ/mol}$$

4. Hydrolysis of acetyl-Coenzyme A



$$\text{Acetyl-CoA} + H_2O \longrightarrow \text{acetate}^- + \text{CoA} + H^+$$

$$\Delta G'^\circ = -31.4\ \text{kJ/mol}$$

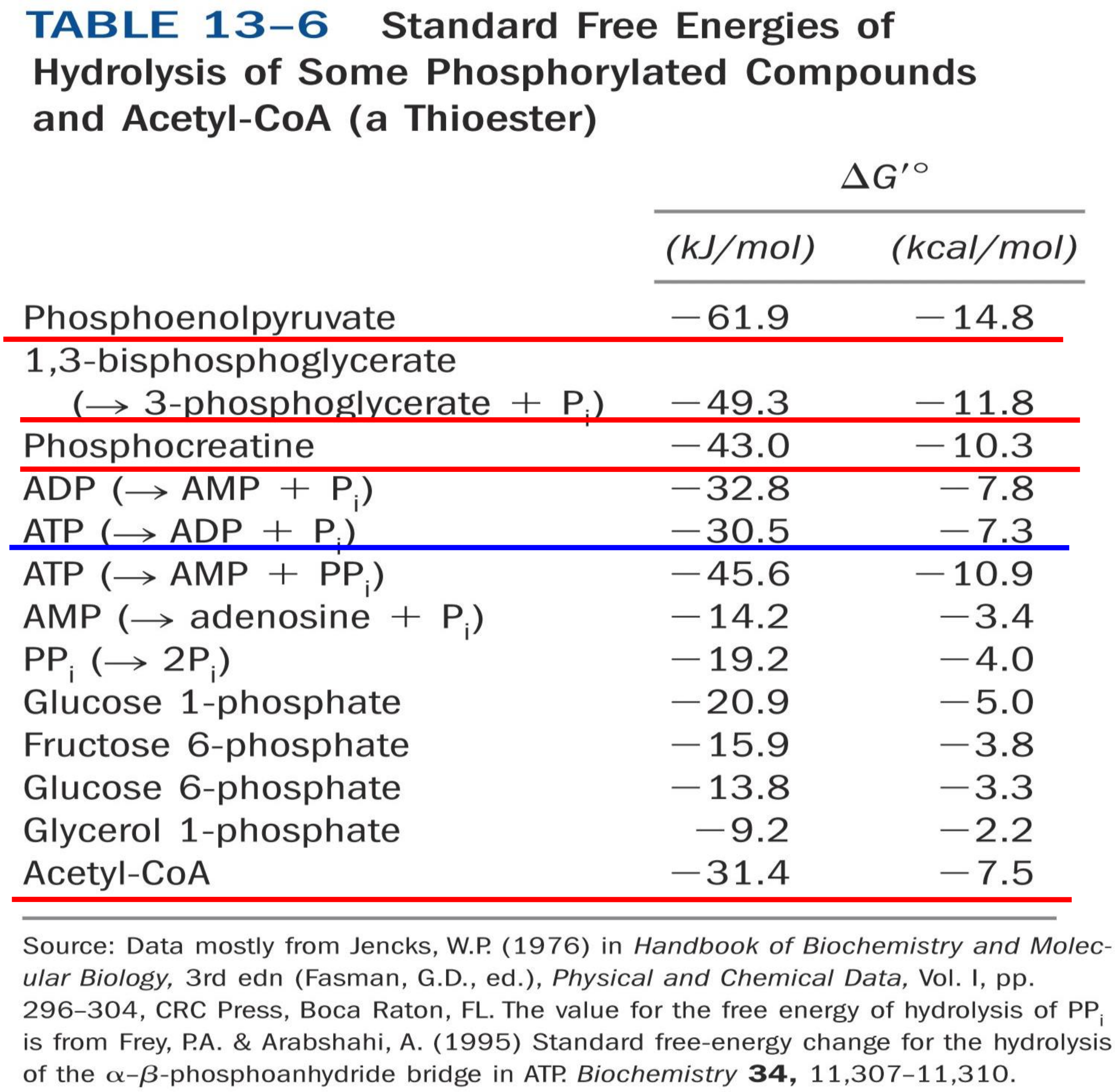


TABLE 13–6 **Standard Free Energies of Hydrolysis of Some Phosphorylated Compounds and Acetyl-CoA (a Thioester)**

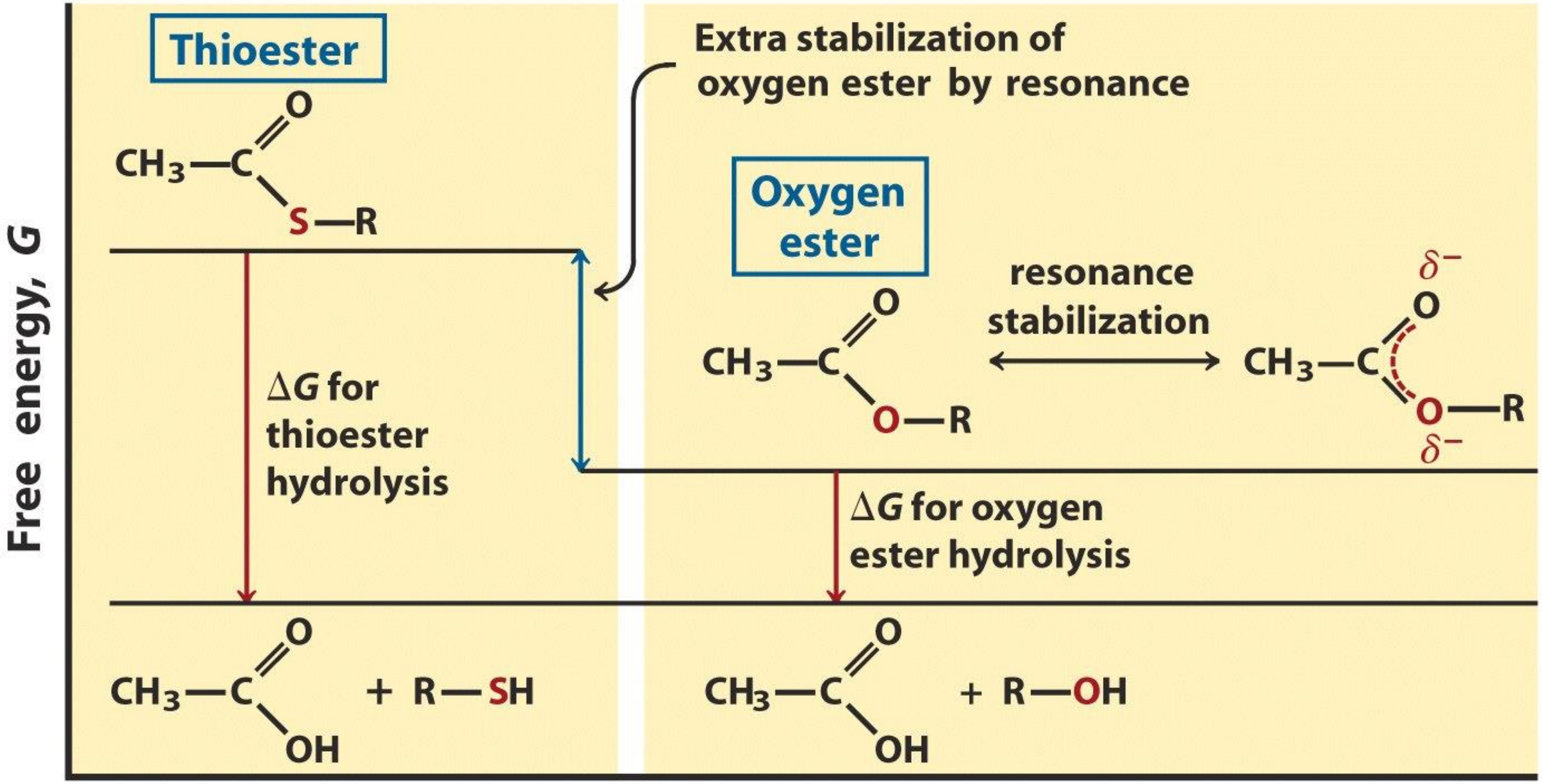
	$\Delta G'^\circ$ (kJ/mol)	$\Delta G'^\circ$ (kcal/mol)
Phosphoenolpyruvate	−61.9	−14.8
1,3-bisphosphoglycerate (→ 3-phosphoglycerate + P_i)	−49.3	−11.8
Phosphocreatine	−43.0	−10.3
ADP (→ AMP + P_i)	−32.8	−7.8
ATP (→ ADP + P_i)	−30.5	−7.3
ATP (→ AMP + PP_i)	−45.6	−10.9
AMP (→ adenosine + P_i)	−14.2	−3.4
PP_i (→ $2P_i$)	−19.2	−4.0
Glucose 1-phosphate	−20.9	−5.0
Fructose 6-phosphate	−15.9	−3.8
Glucose 6-phosphate	−13.8	−3.3
Glycerol 1-phosphate	−9.2	−2.2
Acetyl-CoA	−31.4	−7.5

Source: Data mostly from Jencks, W.P. (1976) in *Handbook of Biochemistry and Molecular Biology,* 3rd edn (Fasman, G.D., ed.), *Physical and Chemical Data,* Vol. I, pp. 296–304, CRC Press, Boca Raton, FL. The value for the free energy of hydrolysis of PP_i is from Frey, P.A. & Arabshahi, A. (1995) Standard free-energy change for the hydrolysis of the α–β-phosphoanhydride bridge in ATP. *Biochemistry* **34,** 11,307–11,310.

Free energy of hydrolysis for thioester and oxygen esters

acetyl-CoA; donor of acyl groups, Feeding two-carbon units into metabolic pathways

Synthesis of fatty acids



$CH_3-C(=O)-S-R$

$CH_3-C(=O)-O-R$

$CH_3-C(=O)-OH + R-SH$

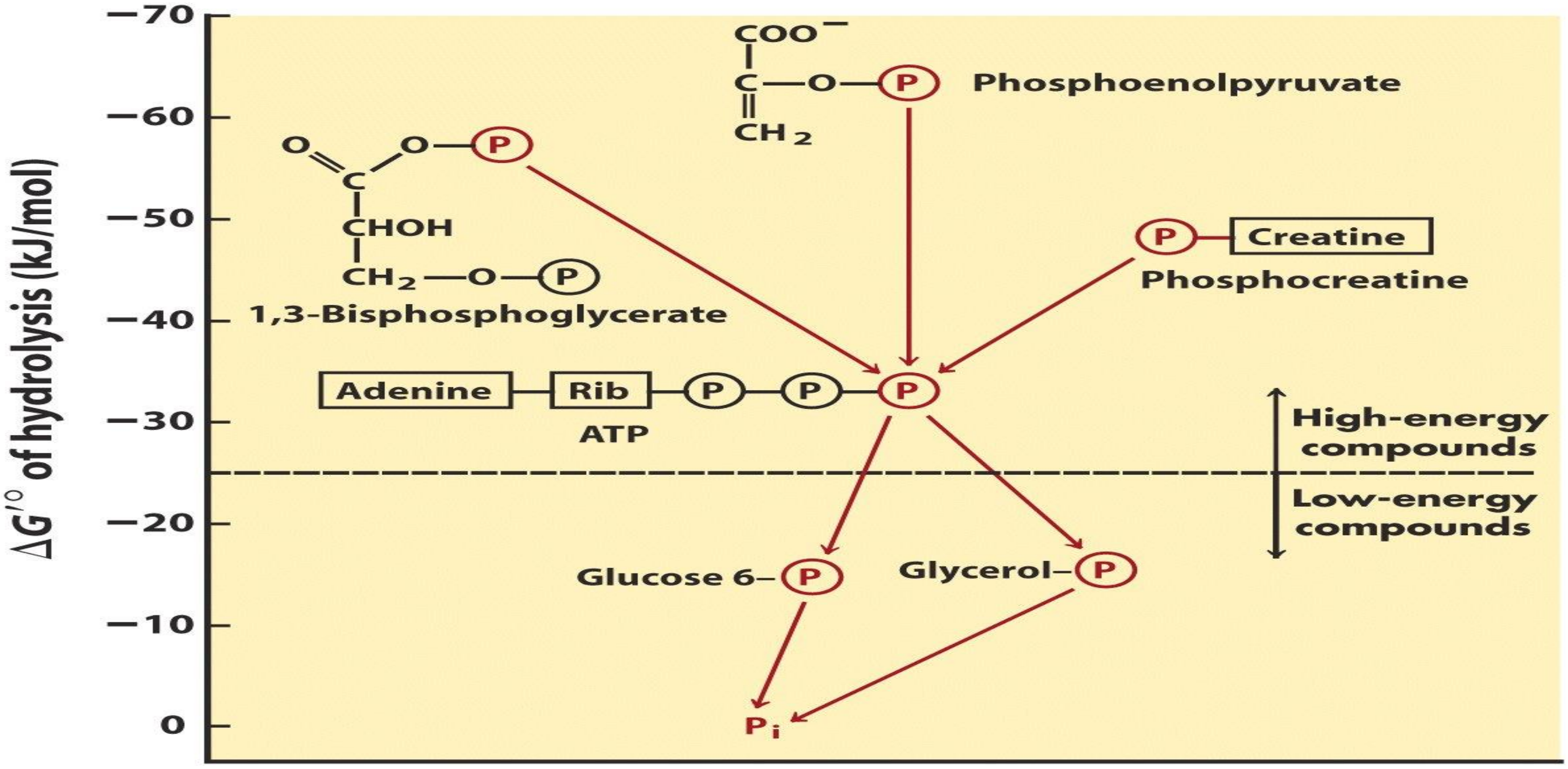
$CH_3-C(=O)-OH + R-OH$

Summary for hydrolysis reactions with large, negative $\Delta G^{o\prime}$

The products are more stable than the reactant by:

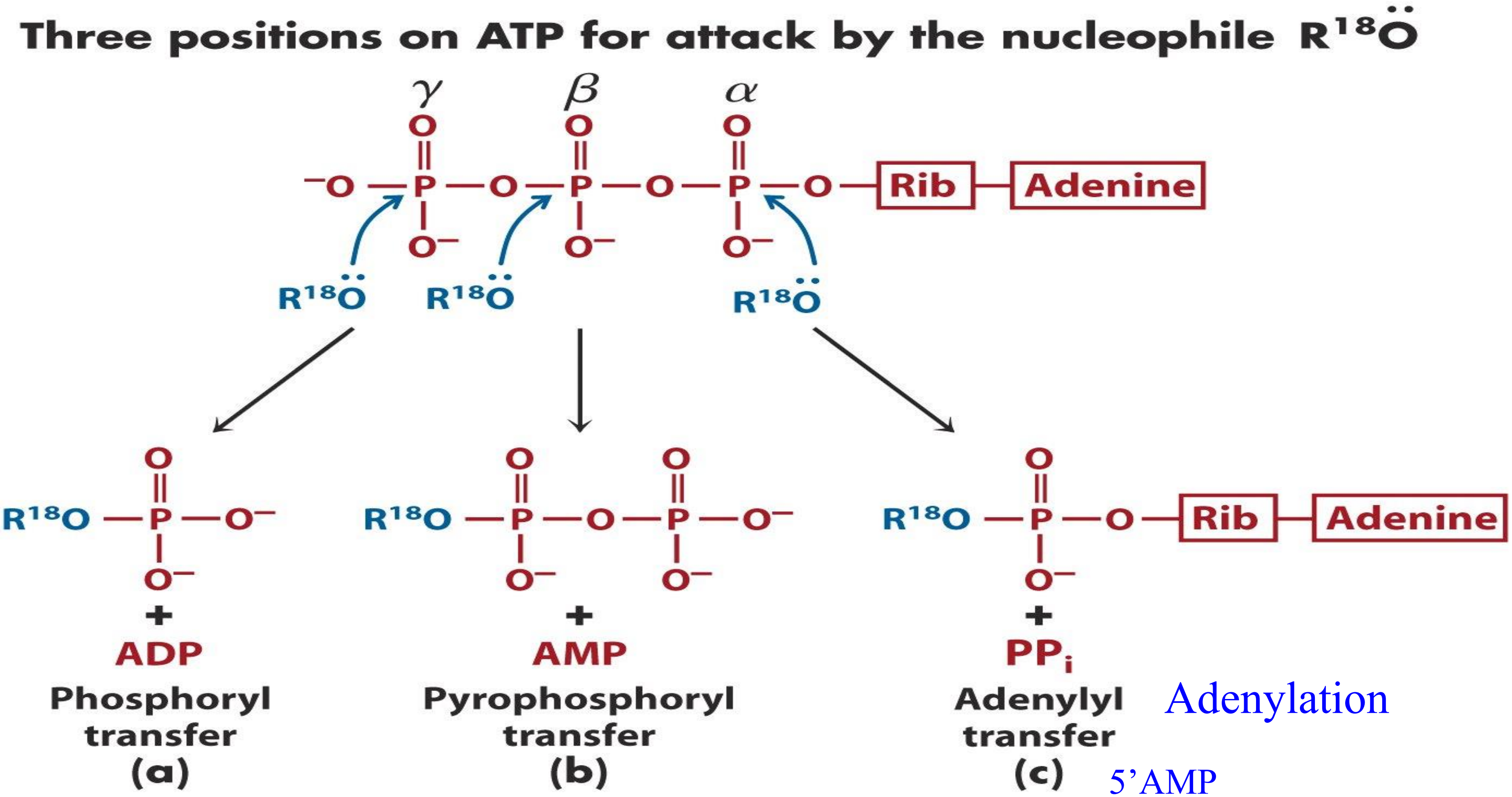
(1) charge separation relieve electrostatic repulsion
(2) product stabilization by ionization
(3) by isomerization (tautomerization)
(4) by resonance stabilization

Ranking of biological phosphate compounds by standard free energy of hydrolysis



ATP: Intermediate position on the scale of group transfer potential
(Universal energy currency)

ATP donates phosphoryl, Pyrophosphoryl, and Adenyl group



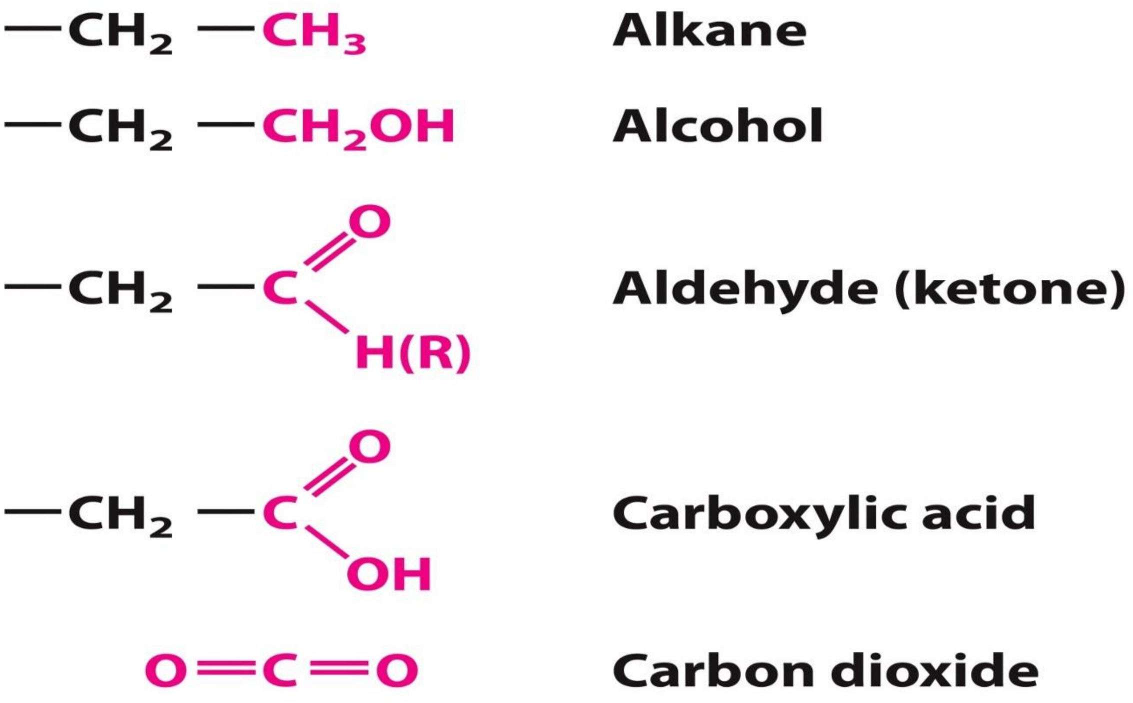
Adenylation

5’AMP

The nucleophile may be an alcohol (R-OH), a carboxy group (R-COOH), or a phosphoanhydride

The oxidation levels of carbon in biomolecules

Reduced organic compounds serve as fuels from which electrons can be stripped off during oxidation.



Each compound is formed by oxidation of the red carbon in the compound shown immediately above. Carbon dioxide is the most highly oxidized form of carbon found in living systems.

Biological oxidation-reduction reactions

- Transfer of phosphoryl group
- Electron transfer in oxidation-reduction reactions
  - Loss of electron: oxidized
  - Gain of electron: reduced

- Source of electron
  - In non-photosynthetic (Food) vs photosynthetic (excited by light)

- Electrons move from metabolic intermediates to specialized electron carriers in enzyme-catalyzed reactions

- The flow of electron can do biological work

  - Electromotive force (emf) → proton-motive force → ATP (chemical work)

Oxidation-Reduction can be described as half-reaction

- Free energy change is also associated with equilibrium with oxidation-reduction reaction

- Oxidation-reduction reaction occur together. It is convenient when describing e- transfer to consider the two halves of an oxidation-reduction reaction separately.

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

1) Fe^{2+} (ferrous) $\rightleftharpoons$ Fe^{3+} (Ferric) + e- : Oxidation reaction

2) Cu^{2+} (cupric)+ e- $\rightleftharpoons$ Cu^{+} : Reduction reaction

; In acid-base reaction, proton donor $\rightleftharpoons$ proton acceptor + H +
An acid and corresponding base function as a conjugated acid-base pair.

; In redox reaction, e- donor (reductant) $\rightleftharpoons$ e- acceptor (oxidant) + e-

- e- donor and corresponding e- acceptor function as a conjugated redox pair

(The e- donating molecules in oxidation-reduction reaction is reducing agent or reductant
The e- accepting molecules is oxidizing agent or oxidant)

Reduction potentials measure affinity for electrons

- When two conjugate redox pairs are together in solution, e- transfer from e- donor of one pair to e- acceptor of other, may proceed spontaneously. The tendency for such a reaction depends on relative affinity of e-acceptor of each redox pair for electrons.

- **Redox couple: couple of oxidant and reductant**

- **Standard reduction potential (표준환원전위, E^{o})**: a measure (in volts) of this affinity (measure in which e- donor loss electron ; electron donor 가 전자를 잃어버리는 경향의 척도)

; Redox couple with large negative E'^{o} provide electron redox couple with large positive E'^{o}

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

n: the number of e- transferred in the reaction
F: faraday's constant
$\Delta E'^{o}$: standard reduction potential at pH 7

Standard reduction potentials can be used to calculate free-energy change

▶ Why are reduction potential so useful to the biochemist?
; We can predict the direction in which electron will tend to flow when components of both half-cells are present in the same solution.

▶ Electron tend to flow to half-cell with more positive E and strength of that tendency is proportional to ΔE, difference in reduction potential.

▶ The energy made available by spontaneous e- flow (free energy change, ΔG) is proportional to ΔE

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

n: the number of e- transferred in the reaction

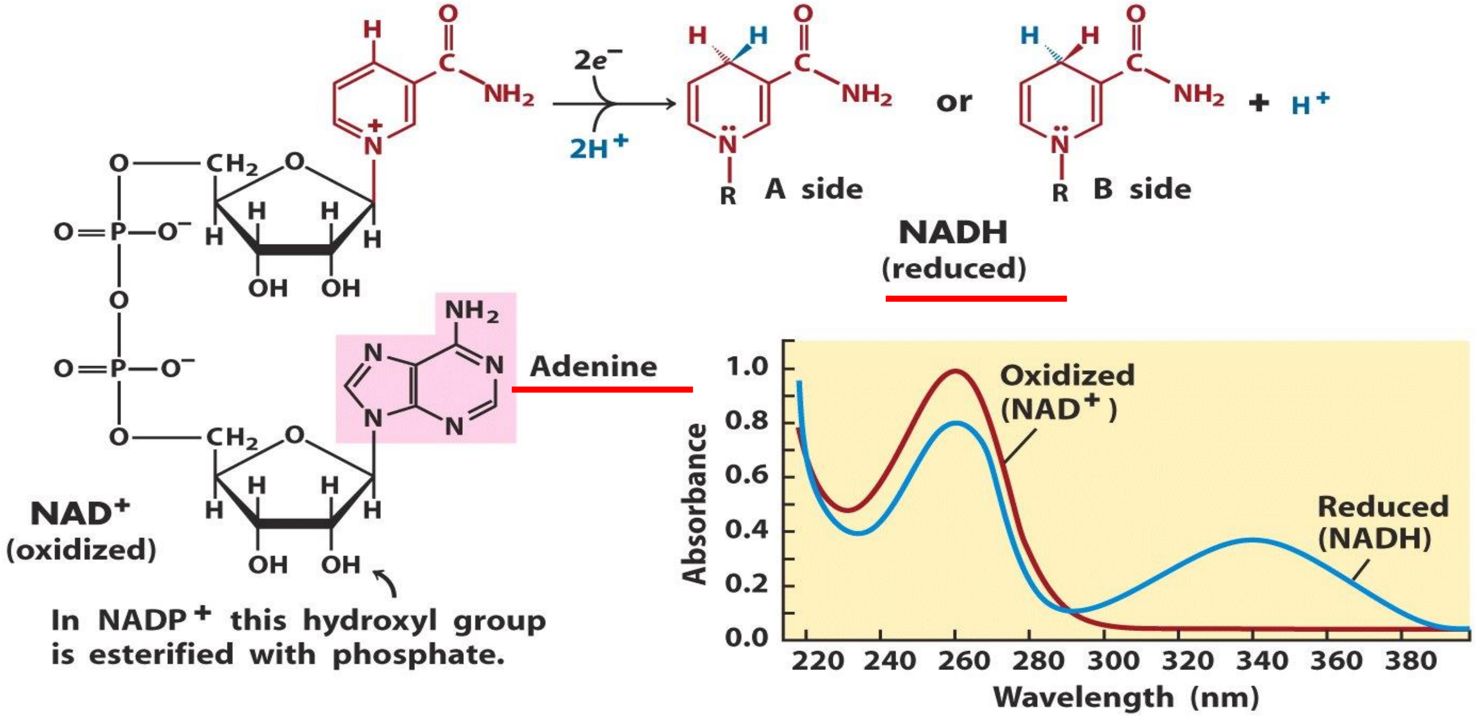
F: faraday's constant

$\Delta E'^{o}$: standard reduction potential at pH 7

▶ Redox couple with large negative E'^{o} provide electron redox couple with large positive E'^{o}

- Cellular oxidation of glucose to carbon dioxide requires specialized electron carriers
- A few types of coenzymes and proteins serve as universial electron carriers
- NADH and NADPH act with dehydrogenase as soluble electron carriers

Hydride ion is added to either front side (A side) or back side (B side)



Nicotinamide adenine dinucleotide (phosphate) (NAD (P)

In catabolism, reducing equivalent is released from these substrate, often in the form of hydride ion (a proton coupled with two electron, H:-)

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

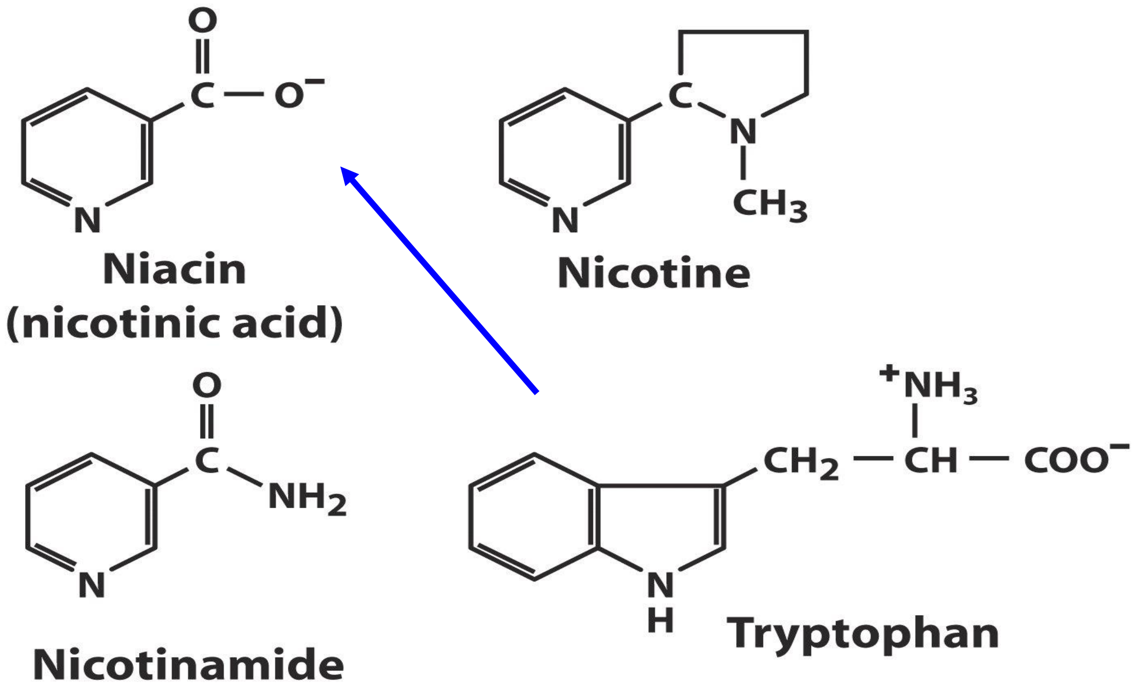
Enzyme	*Coenzyme*	*Stereochemical specificity for nicotinamide ring (A or B)*	*Text page(s)*
Isocitrate dehydrogenase	NAD$^+$	A	610
α-Ketoglutarate dehydrogenase	NAD$^+$	B	610
Glucose 6-phosphate dehydrogenase	NADP$^+$	B	540
Malate dehydrogenase	NAD$^+$	A	612
Glutamate dehydrogenase	NAD$^+$ or NADP$^+$	B	665
Glyceraldehyde 3-phosphate dehydrogenase	NAD$^+$	B	530
Lactate dehydrogenase	NAD$^+$	A	538
Alcohol dehydrogenase	NAD$^+$	A	540

Dietary deficiency of niacin, the vitamin form of NAD and NADP, cause pellagra

- ▶ Pellagra (rough skin): dermatitis, diarrhea, dementia
  → followed in many case by death

- ▶ Individual with diets low in tryptophan content (maize) has niacin deficiency,

  which affect all the NAD(P)-dependent dehydrogenase, causes the serious human disease Pellagra (Italian for rough skin)



Niacin (nicotinic acid)

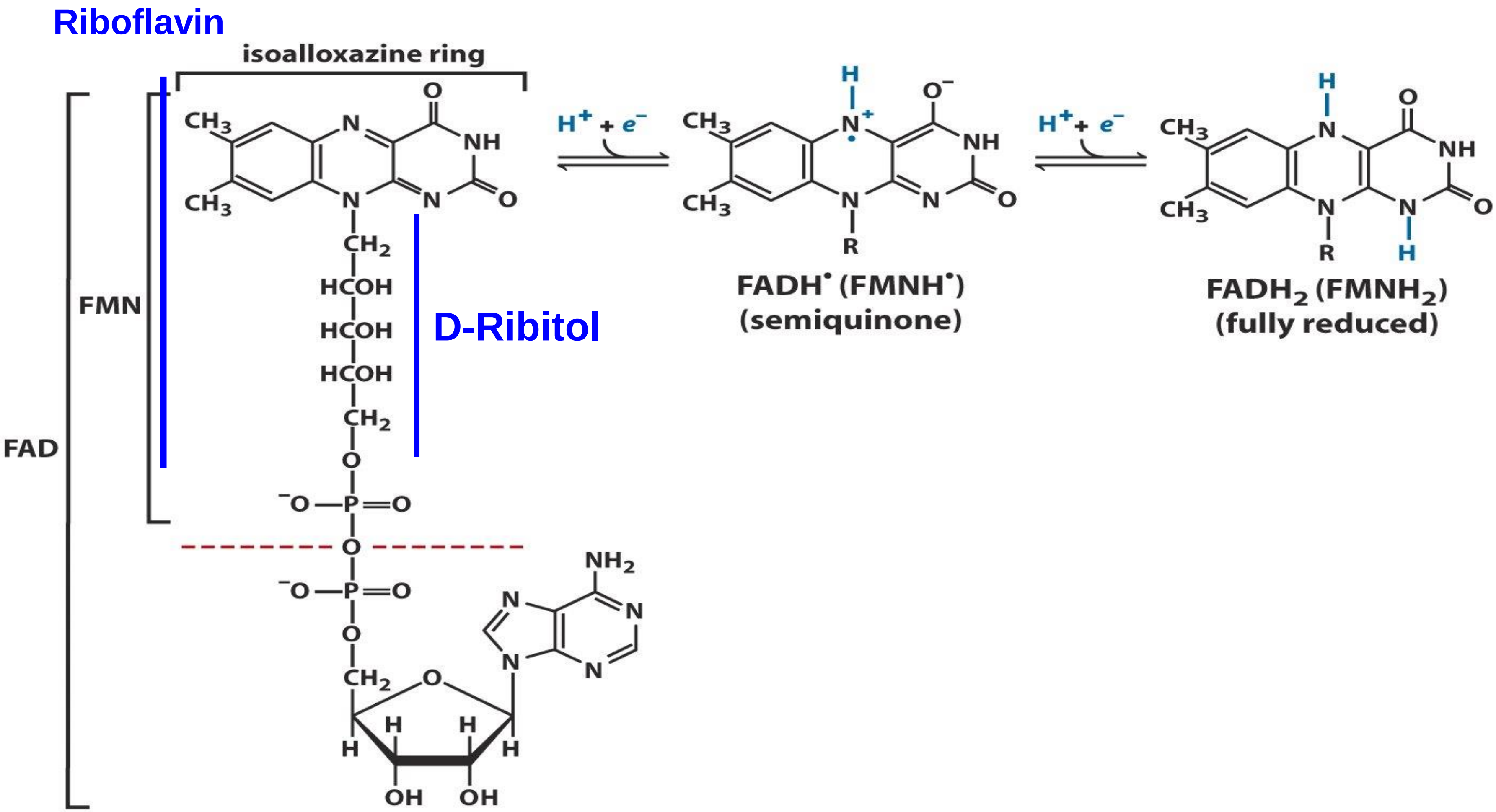
Nicotine

Nicotinamide

Tryptophan

Flavin nucleotide are tightly bound in flavoproteins

Oxidized and reduced FAD and FMN



Flavin adenine dinucleotide (FAD) and
flavin mononucleotide (FMN)

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

Enzyme	*Flavin nucleotide*	*Text page(s)*
Acyl–CoA dehydrogenase	FAD	638
Dihydrolipoyl dehydrogenase	FAD	605
Succinate dehydrogenase	FAD	612
Glycerol 3-phosphate dehydrogenase	FAD	714–715
Thioredoxin reductase	FAD	869
NADH dehydrogenase (Complex I)	FMN	696–697
Glycolate oxidase	FMN	767