NS/201-Biochemistry
Unit IV Topic 14
Bioenergetics
Source Lehninger

Bioenergetics

Living Orgamism

1. **Metabolism**
2. **Reproduction**

Energy: work to survive and reproduce

Energy transduction in biological system

- **Bioenergetics**
  - The quantitative study of…
    - Cellular energy transduction
    - Nature and function of the chemical processes for energy transductions
- **Fundamental laws in thermodynamics governing bioenergetics**
  - First law : Energy conservation
  - Second law: Increase in entropy

Metabolism

- Coordinated cellular activity
- Sum of all the chemical transformations in organism

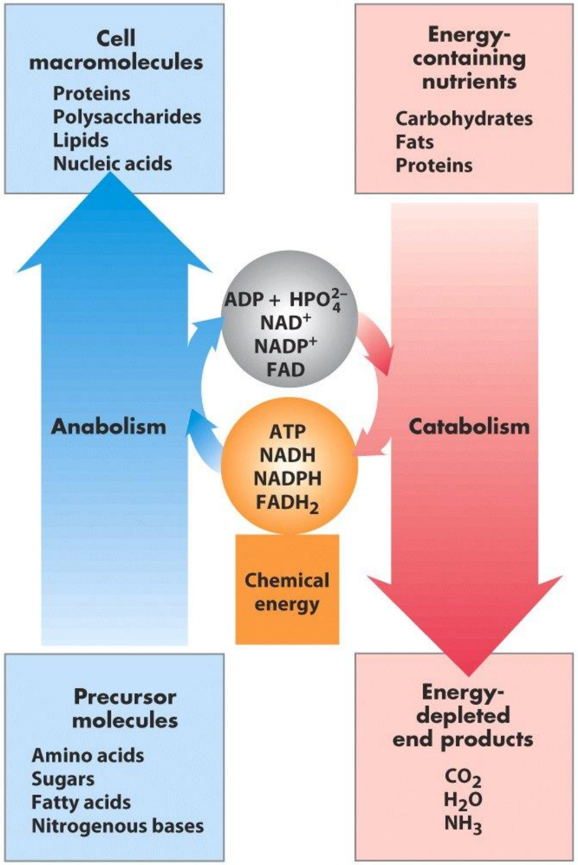
Chemical energy
Precursor molecules
Macromolecules
Specialized biomolecules

Catabolism

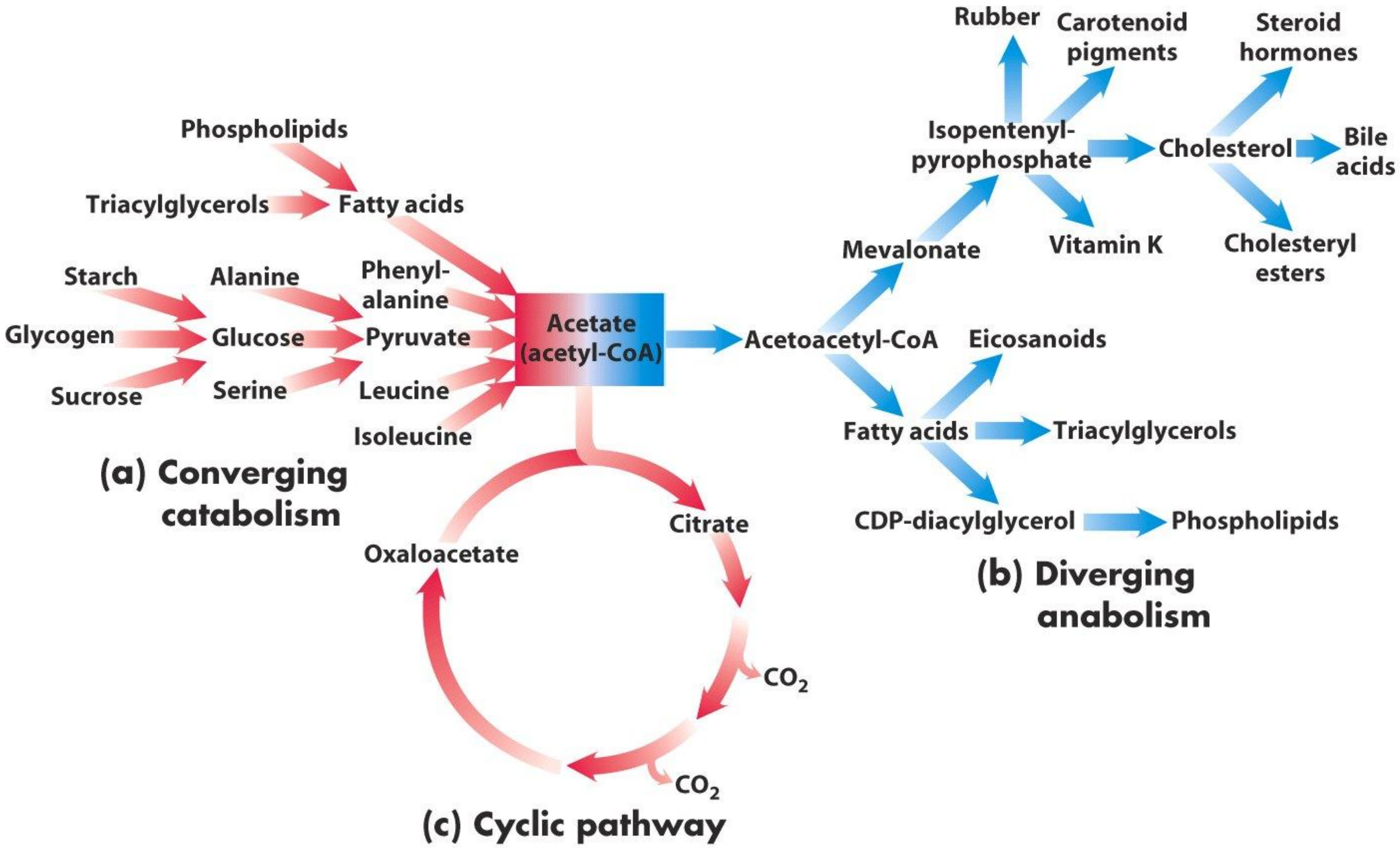
- Degradative phase
- Energy release (exergonic)

Anabolism

- Biosynthesis
- Energy input (endergonic)



Three types of metabolic pathways



13.1 Bioenergetics and Thermodynamics

Free Energy Change for Biological Reactions

- **Thermodynamic quantities describing the energy changes in chemical reaction**
  - Gibbs free energy, ***G***
    - The amount of energy capable of doing work during a reaction at constant T and P
    - Positive ΔG : endergonic
    - Negative ΔG : exergonic, spontaneous reaction
  - Enthalpy, ***H***
    - The heat content of the reacting system
    - Number & kinds of chemical bonds in the reactants and products
    - Positive ΔH : endothermic
    - Negative ΔH : exothermic
  - Entropy, ***S***
    - Quantitative expression for the randomness or disorder in a system
- $\Delta G = \Delta H - T\Delta S$
- **Cells use free energy for reactions**
  - Energy source
    - Heterotrope :Nutrient
    - Autotrope: Solar energy

Standard Free Energy Change vs. Equilibrium Constant

- **aA + bB → cC + dD**
  - Equilibrium constant $$K_{eq} = \frac{[C_{eq}]^c\,[D_{eq}]^d}{[A_{eq}]^a\,[B_{eq}]^b}$$
  - ΔG^o : standard free energy change (J/mol)
    - 298K=25°C, 1M of initial reactants and products,1 atm (101.3 kPa)
  - Standard transformed constants
    - pH 7, 55.5M water, 1mM Mg^{2+} (ATP as reactant)
    - $\Delta G'^o$, K'_{eq}
- **$\Delta G'^o = -RT \ln K'_{eq}$**
  - Spontaneous reaction
    - K''_{eq} >1
    - ΔG^o : negative

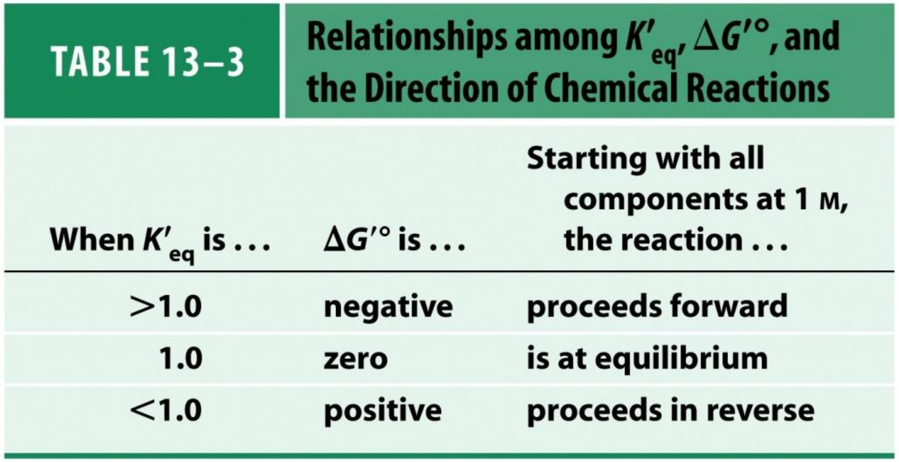


TABLE 13–3 Relationships among K'_{eq}, $\Delta G'^{\circ}$, and the Direction of Chemical Reactions

When K'_{eq} is . . .	$\Delta G'^{\circ}$ is . . .	Starting with all components at 1 M, the reaction . . .
>1.0	negative	proceeds forward
1.0	zero	is at equilibrium
<1.0	positive	proceeds in reverse

Table 13-3
Lehninger Principles of Biochemistry, Fifth Edition
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$\Delta G'^{o}$ for some representative chemical reactions

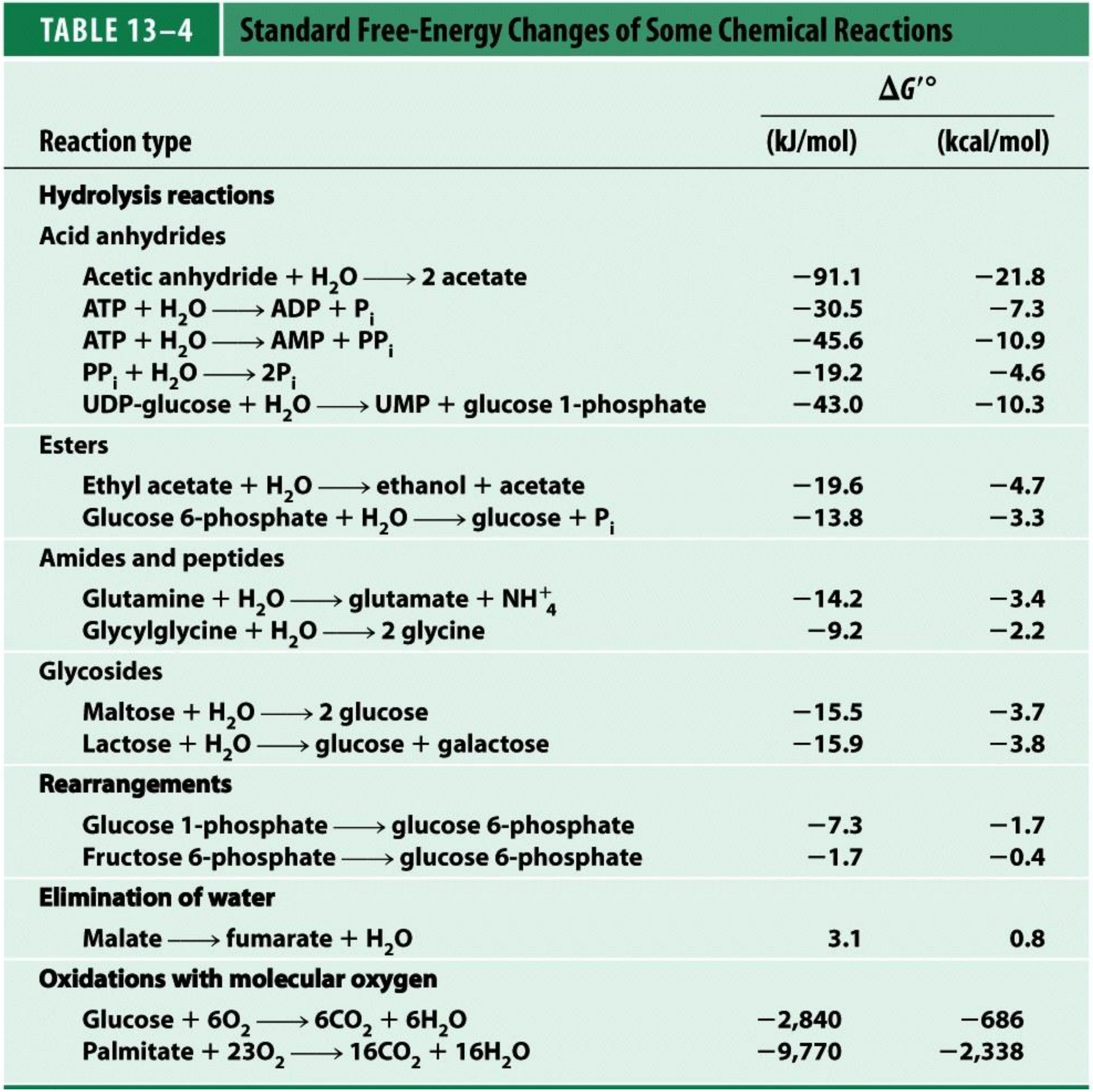


TABLE 13–4 Standard Free-Energy Changes of Some Chemical Reactions

	$\Delta G'^{\circ}$	
Reaction type	**(kJ/mol)**	**(kcal/mol)**
Hydrolysis reactions		
Acid anhydrides		
Acetic anhydride + $H_2O \longrightarrow$ 2 acetate	−91.1	−21.8
ATP + $H_2O \longrightarrow$ ADP + P_i	−30.5	−7.3
ATP + $H_2O \longrightarrow$ AMP + PP_i	−45.6	−10.9
PP_i + $H_2O \longrightarrow$ 2P_i	−19.2	−4.6
UDP-glucose + $H_2O \longrightarrow$ UMP + glucose 1-phosphate	−43.0	−10.3
Esters		
Ethyl acetate + $H_2O \longrightarrow$ ethanol + acetate	−19.6	−4.7
Glucose 6-phosphate + $H_2O \longrightarrow$ glucose + P_i	−13.8	−3.3
Amides and peptides		
Glutamine + $H_2O \longrightarrow$ glutamate + NH_4^+	−14.2	−3.4
Glycylglycine + $H_2O \longrightarrow$ 2 glycine	−9.2	−2.2
Glycosides		
Maltose + $H_2O \longrightarrow$ 2 glucose	−15.5	−3.7
Lactose + $H_2O \longrightarrow$ glucose + galactose	−15.9	−3.8
Rearrangements		
Glucose 1-phosphate $\longrightarrow$ glucose 6-phosphate	−7.3	−1.7
Fructose 6-phosphate $\longrightarrow$ glucose 6-phosphate	−1.7	−0.4
Elimination of water		
Malate $\longrightarrow$ fumarate + H_2O	3.1	0.8
Oxidations with molecular oxygen		
Glucose + $6O_2 \longrightarrow 6CO_2 + 6H_2O$	−2,840	−686
Palmitate + $23O_2 \longrightarrow 16CO_2 + 16H_2O$	−9,770	−2,338

$\Delta G'^{o}$ are additive

- **Sequential chemical reactions**
  - (1) A → B : $\Delta G'^{o}_{1}$, K'_{eq1}
    glucose + Pi → G-6P + H_2O ; $\Delta G'^{o}$ = 13.8 kJ/mol
  - (2) B → C : $\Delta G'^{o}_{2}$, K'_{eq2}
    ATP + H_2O → ADP + Pi ;$\Delta G'^{o}$ = -30.5 kJ/mol
  - (1) + (2) : A → C : $\Delta G'^{o}_{1} + \Delta G'^{o}_{1}$, K'_{eq1} X K'_{eq2}
    ATP + glucose → ADP + Pi ; $\Delta G'^{o}$ = -16.7 kJ/mol
  - Coupling of endergonic and exergonic reaction to make exergonic reaction

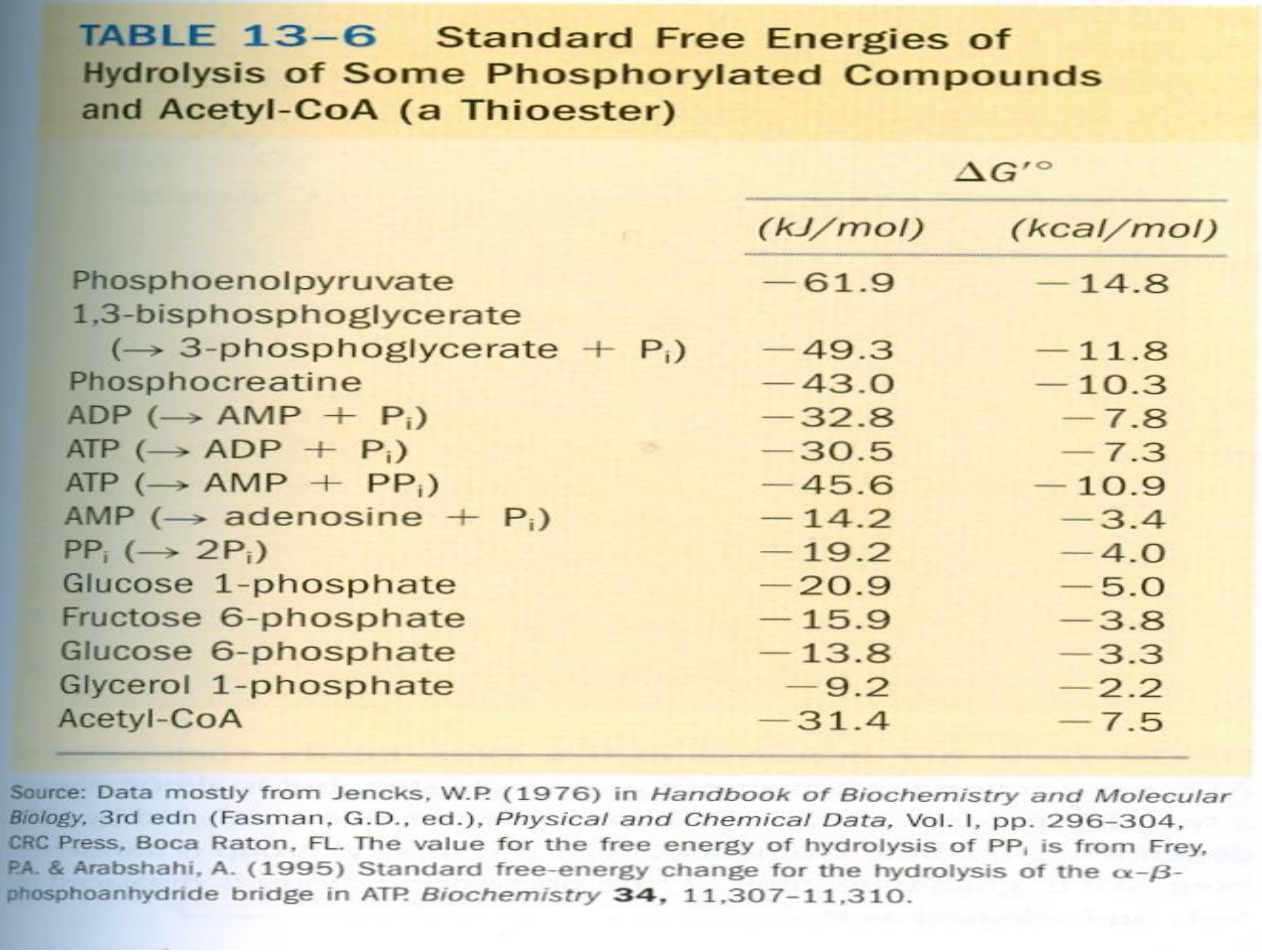


TABLE 13–6 Standard Free Energies of Hydrolysis of Some Phosphorylated Compounds and Acetyl-CoA (a Thioester)

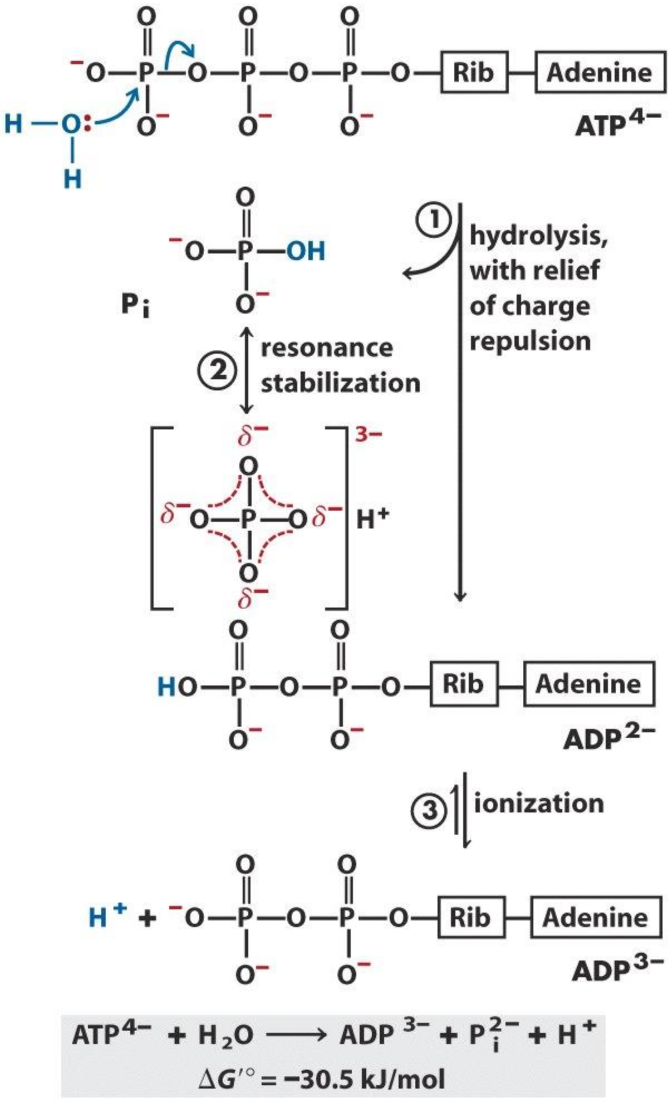
	$\Delta G'^\circ$ (kJ/mol)	$\Delta G'^\circ$ (kcal/mol)
Phosphoenolpyruvate	−61.9	−14.8
1,3-bisphosphoglycerate (→ 3-phosphoglycerate + P_i)	−49.3	−11.8
Phosphocreatine	−43.0	−10.3
ADP (→ AMP + P_i)	−32.8	−7.8
ATP (→ ADP + P_i)	−30.5	−7.3
ATP (→ AMP + PP_i)	−45.6	−10.9
AMP (→ adenosine + P_i)	−14.2	−3.4
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.

13.2 Phosphoryl Group Transfers and ATP

Free-Energy Change for ATP Hydrolysis

- **Chemical basis for large & negative $\Delta G'^{o}$ for ATP hydrolysis**
  - Relief of electrostatic repulsion
  - Resonance stabilization of released P_i
  - Ionization of ADP^{2-} to release H^+
  - Greater degree of solvation of the P_i and ADP than ATP
  - Products concentrations are far below the concentration at equilibrium→ mass action favors hydrolysis of ATP



$$ATP^{4-} + H_2O \longrightarrow ADP^{3-} + P_i^{2-} + H^+$$

$$\Delta G'^{\circ} = -30.5 \text{ kJ/mol}$$

- **ΔG_p : phosphorylation potential in the cell**
  - in human erythrocyte
  - $\Delta G_p = \Delta G'^{o} + RT \ln [ADP][Pi]/[ATP]$
    $= -30.5 \text{ kJ/mol} - 21 \text{ kJ/mol} = -52 \text{ kJ/mol}$

Free-Energy Change for ATP Hydrolysis

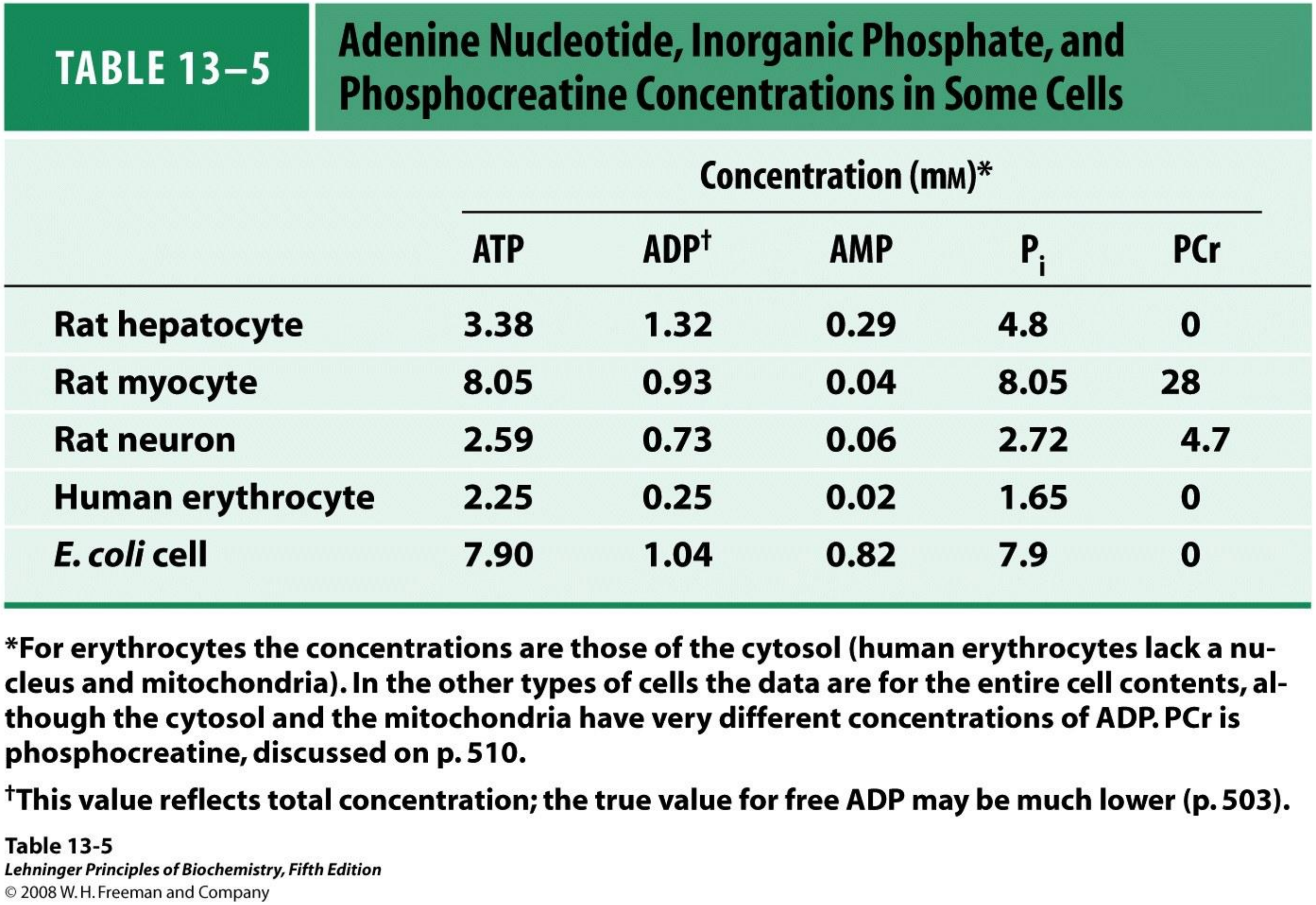


TABLE 13–5 Adenine Nucleotide, Inorganic Phosphate, and Phosphocreatine Concentrations in Some Cells

	Concentration (mM)*				
	ATP	ADP[†]	AMP	P_i	PCr
Rat hepatocyte	3.38	1.32	0.29	4.8	0
Rat myocyte	8.05	0.93	0.04	8.05	28
Rat neuron	2.59	0.73	0.06	2.72	4.7
Human erythrocyte	2.25	0.25	0.02	1.65	0
E. coli cell	7.90	1.04	0.82	7.9	0

*For erythrocytes the concentrations are those of the cytosol (human erythrocytes lack a nucleus and mitochondria). In the other types of cells the data are for the entire cell contents, although the cytosol and the mitochondria have very different concentrations of ADP. PCr is phosphocreatine, discussed on p. 510.

[†] This value reflects total concentration; the true value for free ADP may be much lower (p. 503).

Table 13-5
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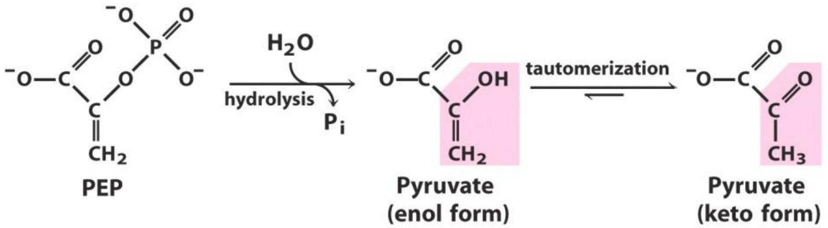
Phosphorylated compounds

- Phosphoenolpyruvate
- 1,3-bisphosphoglycerate
- Phosphocreatine
- ADP
- ATP
- AMP
- PPi
- Glucose 1-phosphate
- Fructose 6-phosphate
- Glucose 6-phosphate

Other High Energy Compounds : Phosphorylated Compounds

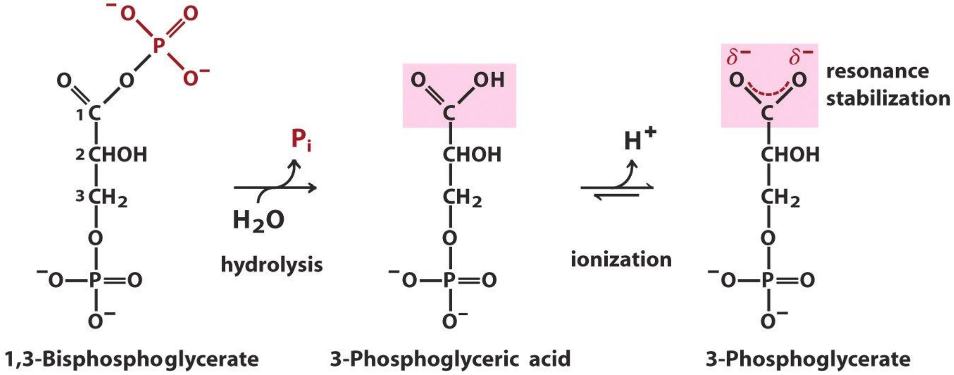
- **Phosphoenolpyruvate**
  - Stabilization of product by tautomerization
  - $\Delta G'^{o}$ = - 61.9 kJ/mol



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

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

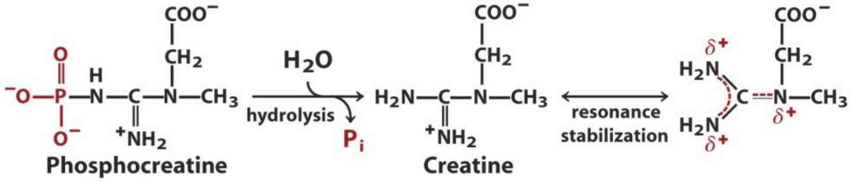
- **1,3-bisphosphoglycerate**
  - Stabilization by ionization of a direct product (3-phosphoglycerate)
  - Resonance stabilization of the ionized product
  - $\Delta G'^{o}$ = - 49.3 kJ/mol



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

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

- **Phosphocreatine**
  - Resonance stabilization of a product
  - $\Delta G'^{o}$ = - 43.0 kJ/mol

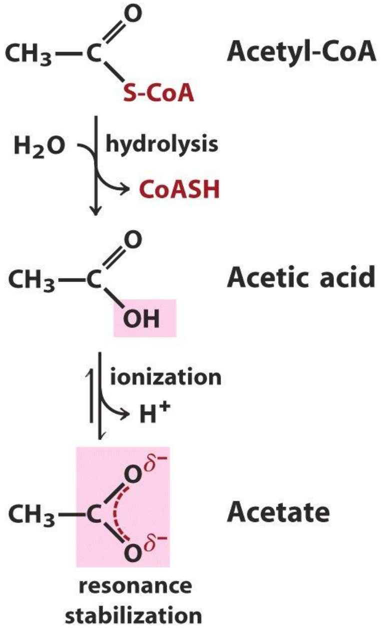


$Phosphocreatine^{2-} + H_2O \longrightarrow creatine + P_i^{2-}$

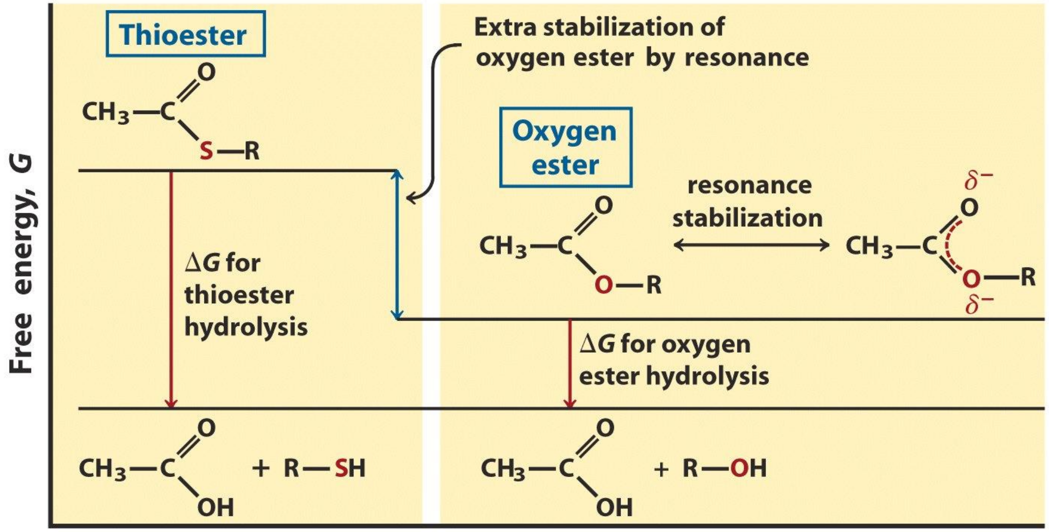
$\Delta G'^{\circ} = -43.0$ kJ/mol

Other High Energy Compounds : Thioesters

- **Thioester**
  - S instead of O in the ester bond
  - Resonance stabilization of hydrolysis product
  - Less resonance stabilization than ester
    - Large free energy difference between thioester and the hydrolysis product

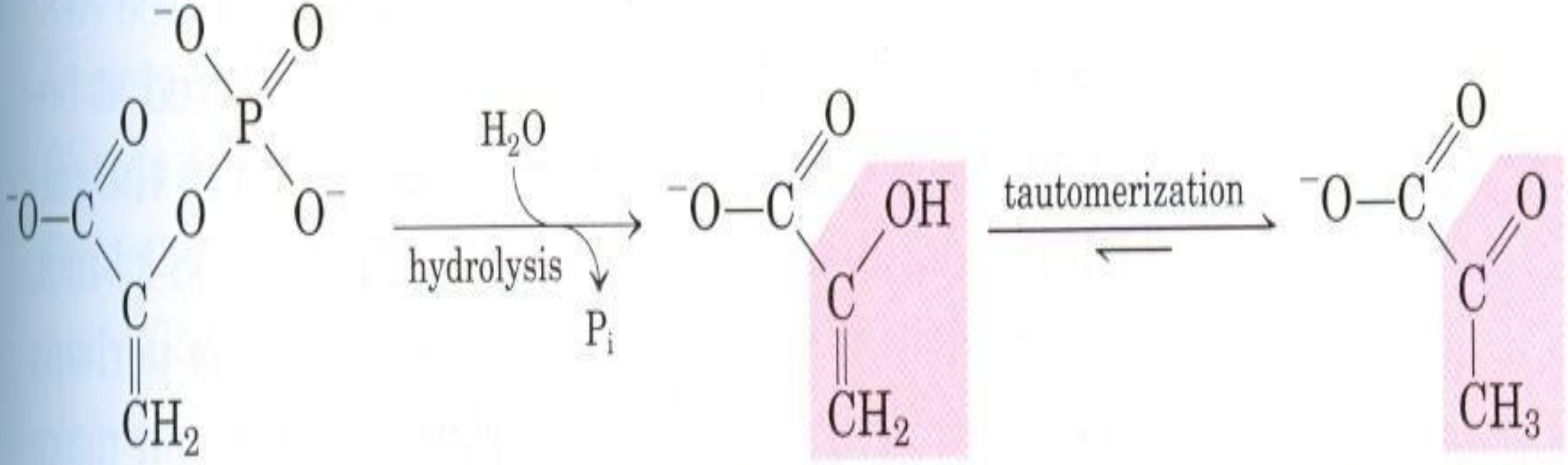


$$\text{Acetyl-CoA} + H_2O \longrightarrow \text{acetate}^- + \text{CoA} + H^+$$
$$\Delta G'^\circ = -31.4 \text{ kJ/mol}$$



Phosphoenolpyruvate

- Phosphoenolpyruvate contains a phosphate ester bond that undergoes to yield to enol form of pyruvate
- The enol form of pyruvate can immediately tautomerize to the more stable keto form of pyruvate. Because phosphoenolpyruvate has only one form (enol) and the product, pyruvate, has two possible forms, the product is more stabilized relative to the reactant.
- This is the greatest contributing factor to the high standard free energy change of hydrolysis of phosphoenolpyruvate ($\Delta G'^{0}$ = -61,9 kj/mol)



PEP

Pyruvate
(enol form)

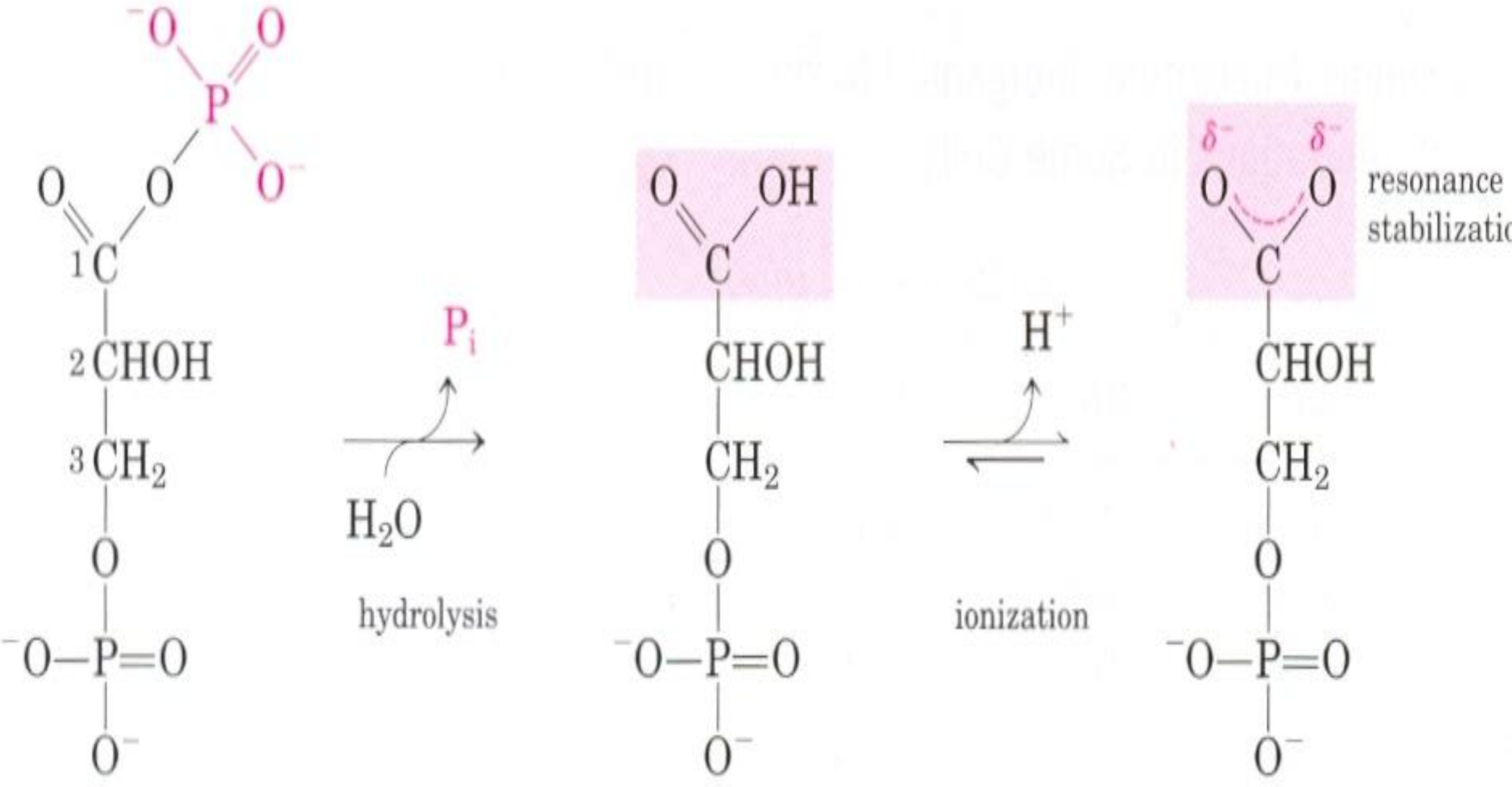
Pyruvate
(keto form)

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

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

- 1,3-bisphosphoglycerate contains an anhydride bond between the carboxyl group at C-1 and phosphoric acid.
- Hydrolysis of this acyl phosphate is accompanied by a large, negative, standard free energy change ($\Delta G'^{0}$ = -49,3 kj/mol)
- This large, negative $\Delta G'^{0}$ can, again, be explained in terms of the structure of reactants and products
-

- When the water is added to anhyhride bond of 1,3-bisphosphoglycerate, one of the direct products, 3-phosphoglyceric acid, can immediately lose a proton to give the carboxylate ion, 3-phosphoglycerate, which has two equally probable resonance forms
- Removal of a direct product, 3-phospho-glyceric acid, and formation of resonance-stabilized ion favor the forward reaction.



1,3-Bisphosphoglycerate

3-Phosphoglyceric acid

3-Phosphoglycerate

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

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

Phosphocreatine

- In the phosphocreatine, the P-N bond can be hydrolyzed to generate free creatine and P_i. The release of P_i and the resonance stabilization of creatine favor the forward reaction. The standard free energy change of phosphocreatine is large and negative ($\Delta G'^0 = -49.3$ kj/mol).

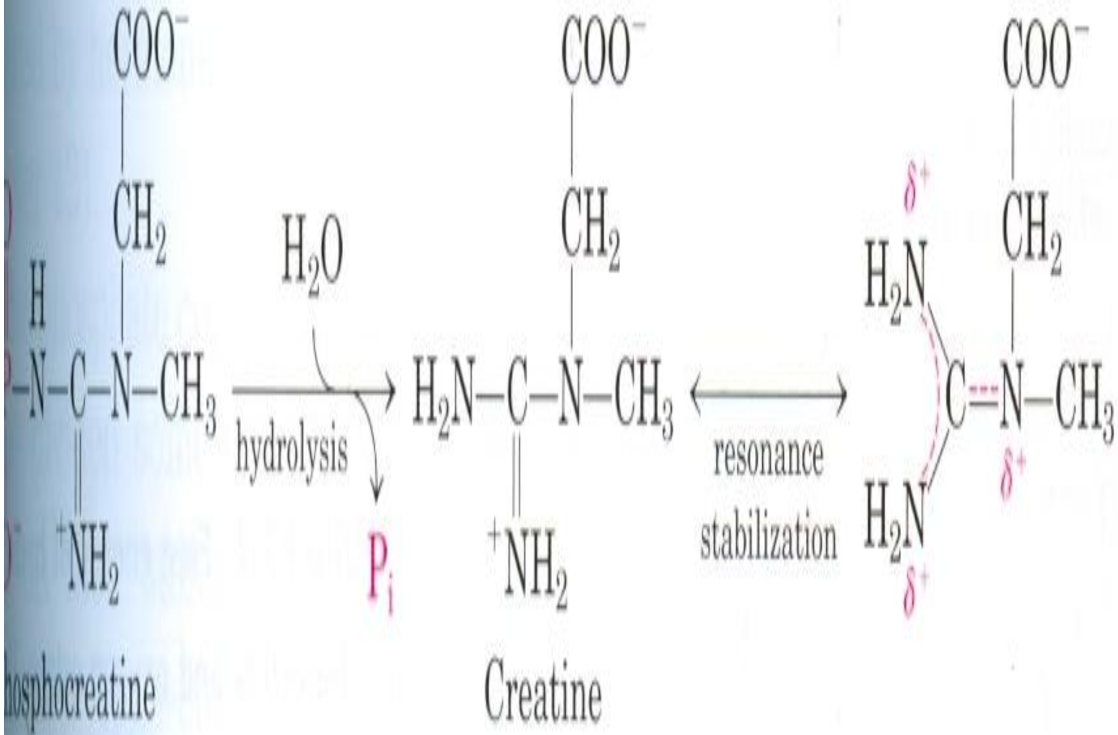


FIGURE 13-5 Hydrolysis of phosphocreatine. Breakage of the P—N bond in phosphocreatine produces creatine, which is stabilized by formation of a resonance hybrid. The other product, P_i, is also resonance stabilized.

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

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

- In thioesters a sulfur atom is replaced the usual oxygen in the ester bond
- Thioesters have large, negative standard free energy change of hydrolysis.
- Acetyl coenzyme A is one of many thioesters important in metabolism. The acyl group in these compounds is activated for trans-acylation, condensation or oxidation-reduction reactions.

- Hydrolysis of the ester bond generates a carboxylic acid which can ionize and assume several resonance forms.
- $\Delta G'^{0}$ = -31.4 kj/mol for acetyl-CoA hydrolysis

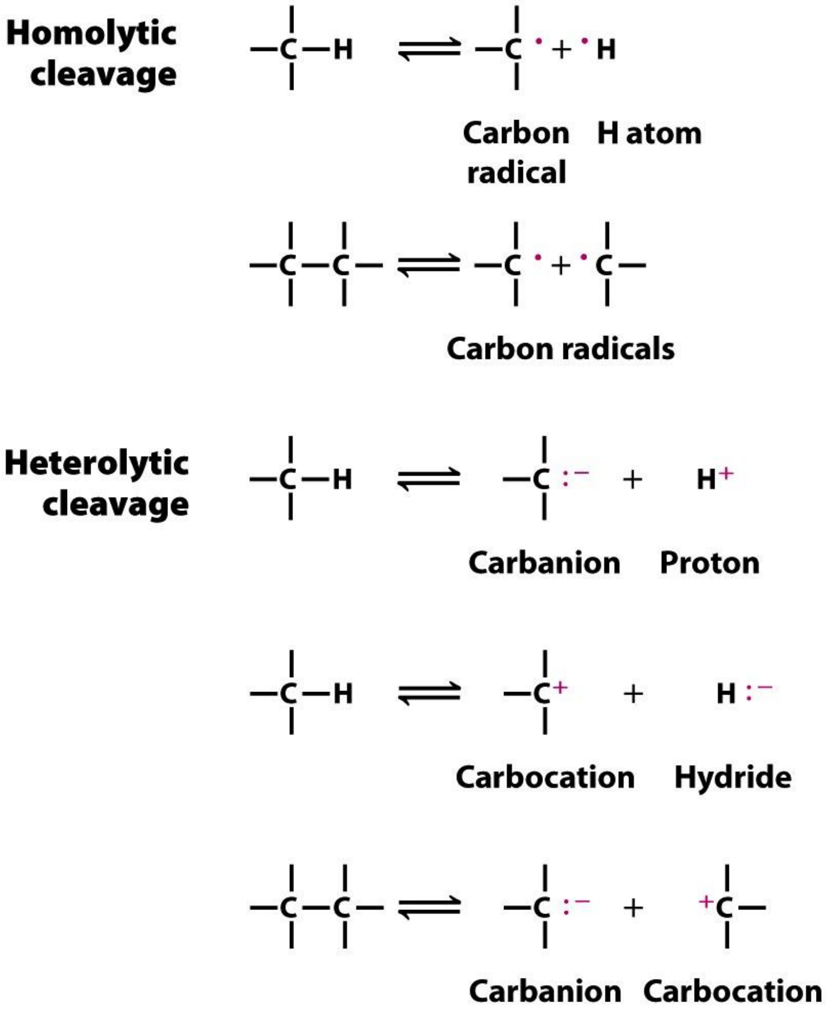
13.2 Chemical logic & common biochemical reactions

General categories of biochemical reactions

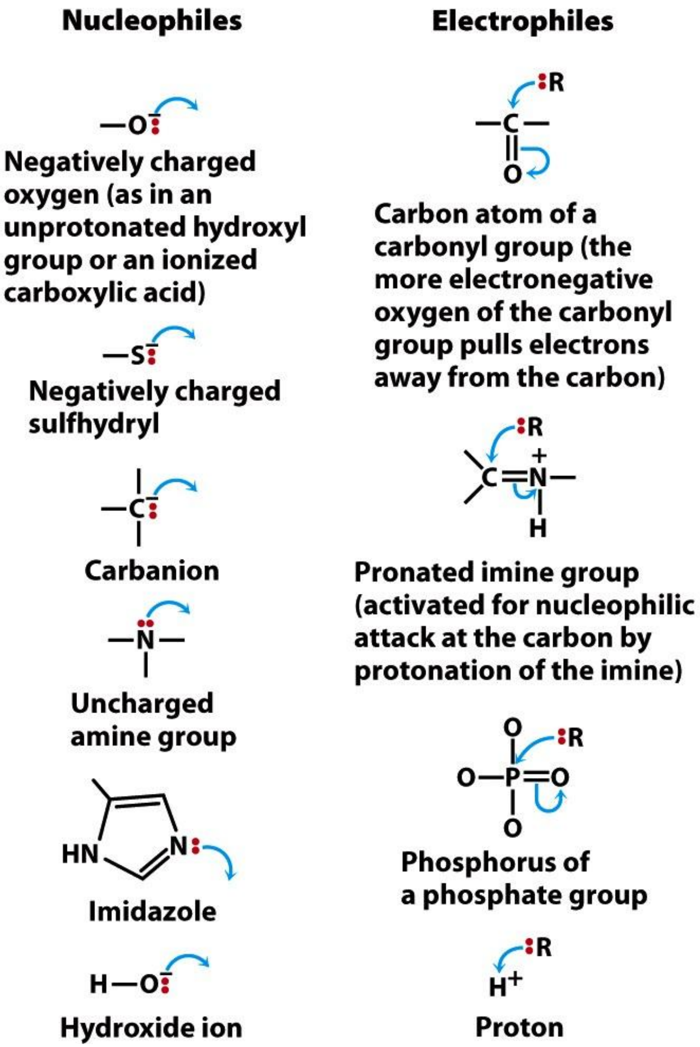
- Reactions that make or break C-C bonds
- Internal rearrangements/ isomerizations/ eliminations
- Free-radical reactions
- Group transfers
- Oxidation-reductions

Two basic chemical principle

Covalent bond breakdown



Nucleophile/ electrophile



Nucleophiles

Negatively charged oxygen (as in an unprotonated hydroxyl group or an ionized carboxylic acid)

Negatively charged sulfhydryl

Carbanion

Uncharged amine group

Imidazole

Hydroxide ion

Electrophiles

Carbon atom of a carbonyl group (the more electronegative oxygen of the carbonyl group pulls electrons away from the carbon)

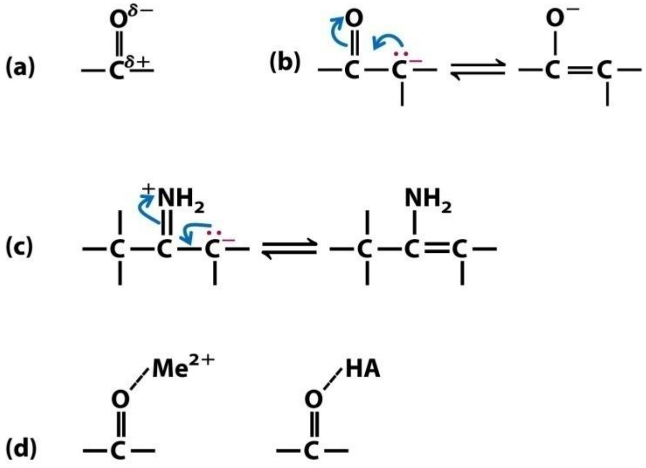
Pronated imine group (activated for nucleophilic attack at the carbon by protonation of the imine)

Phosphorus of a phosphate group

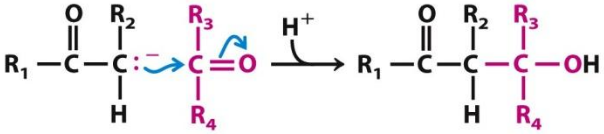
Proton

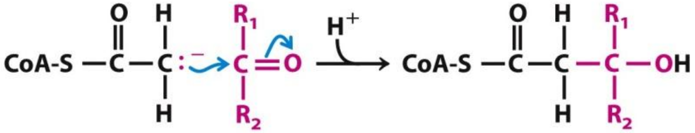
Formation & breakdown of C-C bonds

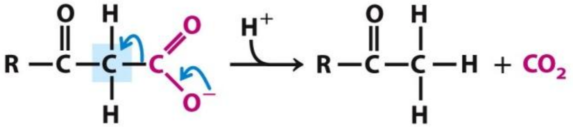
- **Carbanion stabilization**
  - by carbonyl group
  - by imine
  - by metal ions or general acid catalyst



- **Common reactions mediated by carbonyl-stabilized carbanions**


Aldol condensation


Claisen ester condensation


Decarboxylation of a β-keto acid

Formation & breakdown of C-C bonds

- **Carbocation in C-C formation**

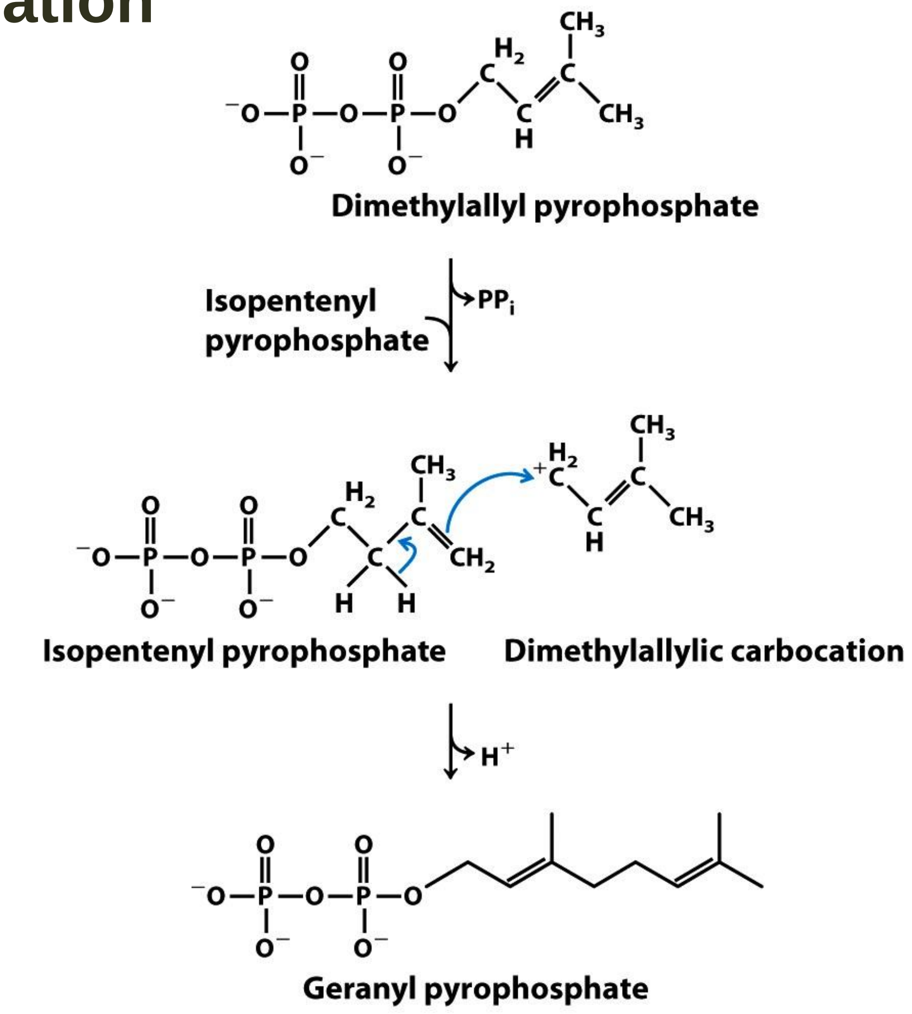


Figure 13-5
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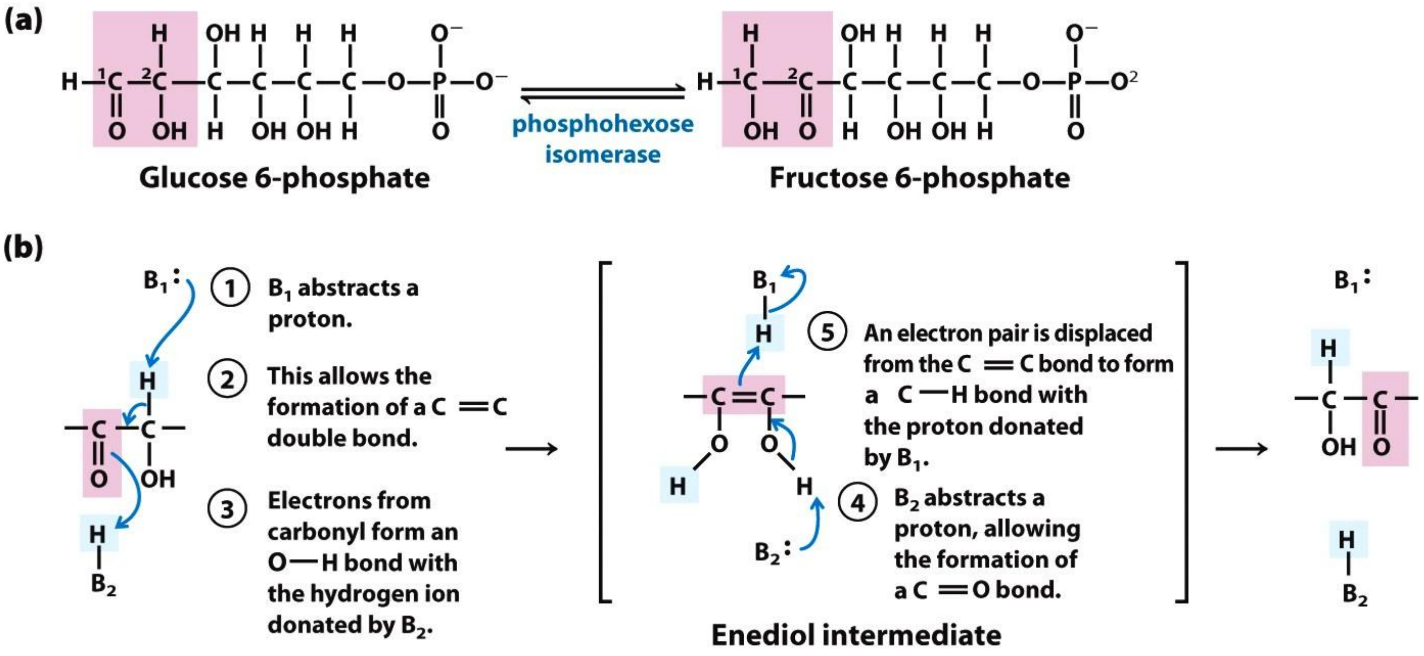
Internal rearrangements, Isomerizations, eliminations

- Rearrangements/ isomerizations



① B_1 abstracts a proton.

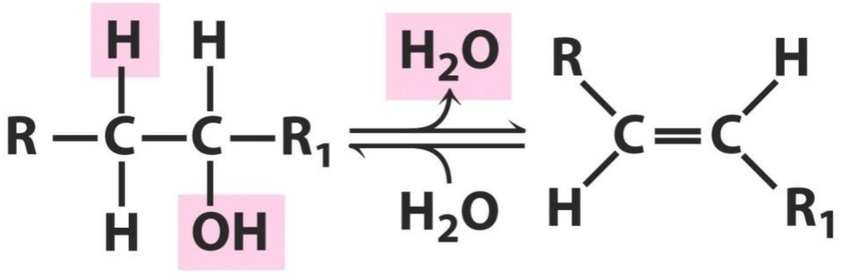
② This allows the formation of a C ═C double bond.

③ Electrons from carbonyl form an O—H bond with the hydrogen ion donated by B_2.

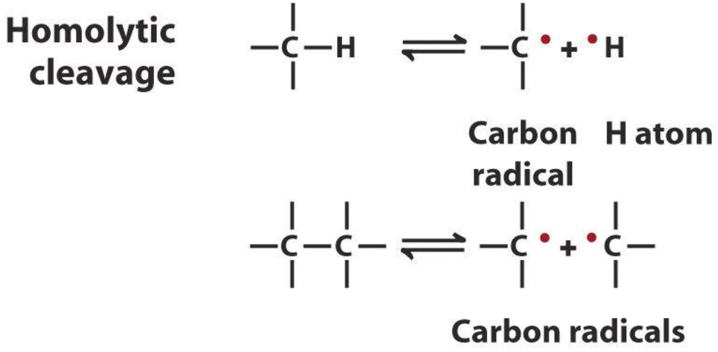
④ B_2 abstracts a proton, allowing the formation of a C ═O bond.

⑤ An electron pair is displaced from the C ═C bond to form a C—H bond with the proton donated by B_1.

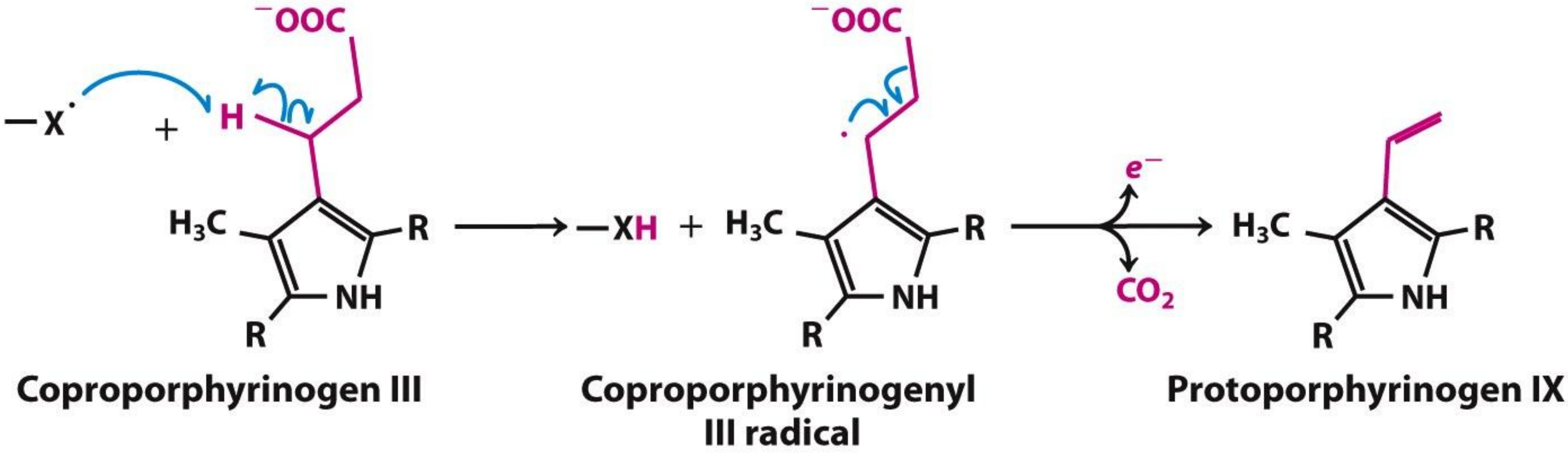
- Elimination reactions



Free radical reactions

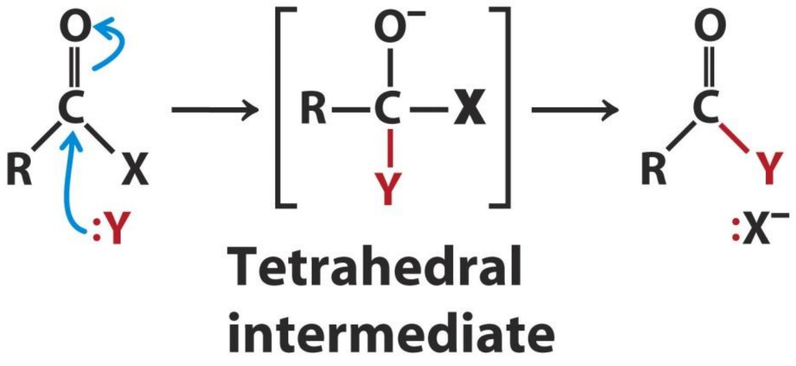


- **Free radical-initiated decarboxylation**

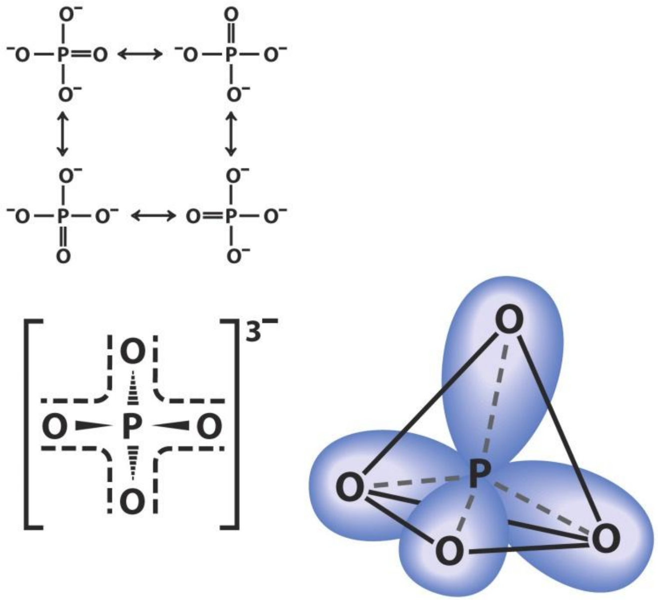


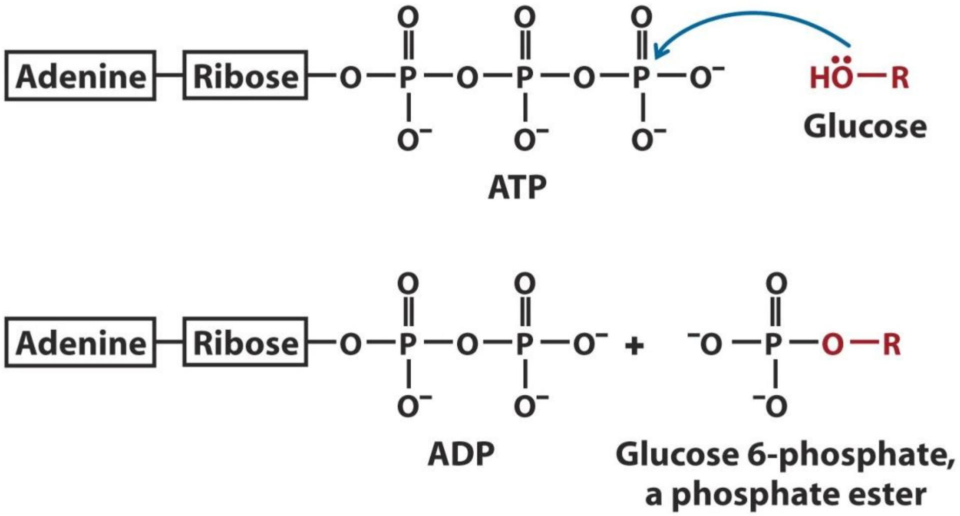
Group transfer reactions

- Acyl group transfer



- Phosphoryl group transfer





Oxidation-reduction reactions

- Oxidation
  - Lose of 2 e^- and 2 H^+ ; dehydrogenations (dehydrogenases)
  - Covalent addition of oxygen to carbon atom (oxidases/ oxygenases)