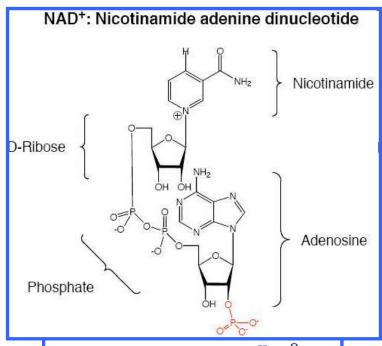
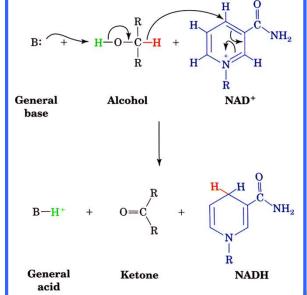
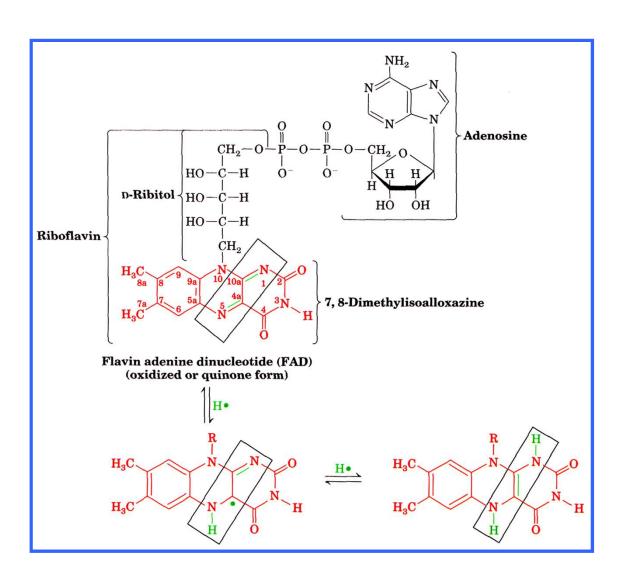
Metabolism: Oxidations and reductions





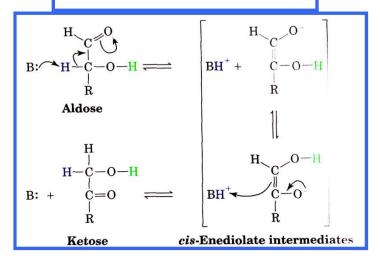




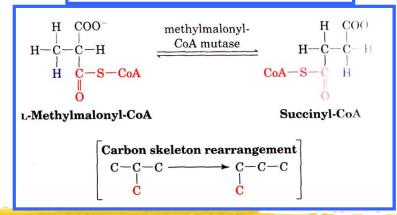
Metabolism: Eliminations, isomerizations, rearrangements

dehydration (a) Concerted $R - C - C - R' \longrightarrow C = C + H^{+} + OH^{-}$ $H \longrightarrow C + H^{+} + OH^{-}$ Stepwise via a carbocation $R - C - C - R' \longrightarrow R - C - C - R' \longrightarrow H$ $R - C - C - R' \longrightarrow R - C - C - R' \longrightarrow H$ $R - C - C - R' \longrightarrow R - C - C - R' \longrightarrow H$ Stepwise via a carbanion $R = C - C - R' \longrightarrow R - C - C - R' \longrightarrow R = C - R' \longrightarrow R$ $H \longrightarrow OH$ $H \longrightarrow OH$

> isomerization



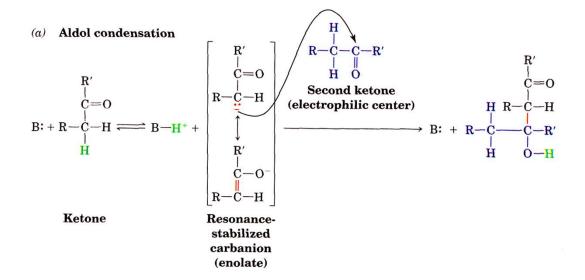
> rearrangement





Metabolism: C-C bond formation and

cleavage



(b) Claisen ester condensation

$$\begin{array}{c} H \quad O \\ \vdots C - C - SCoA \\ H \\ \end{array}$$

$$B: + \begin{array}{c} H \quad O \\ \vdots C - C - SCoA \\ H \\ \end{array}$$

$$Addition to \\ electrophilic \\ center [as \\ in (a)] \\ \end{array}$$

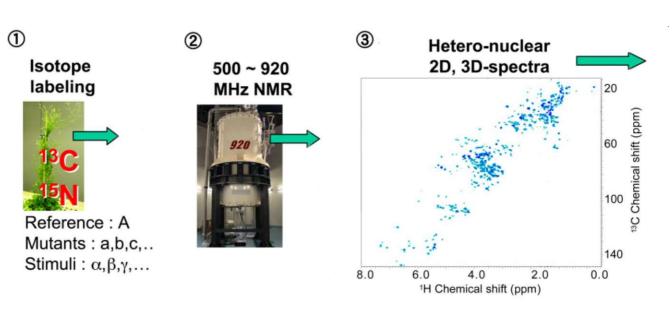
$$Addition to \\ electrophilic \\ center [as \\ in (a)]$$

Resonance-stabilized enolate

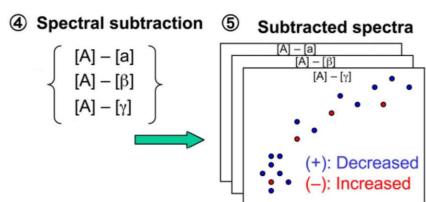
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enolate

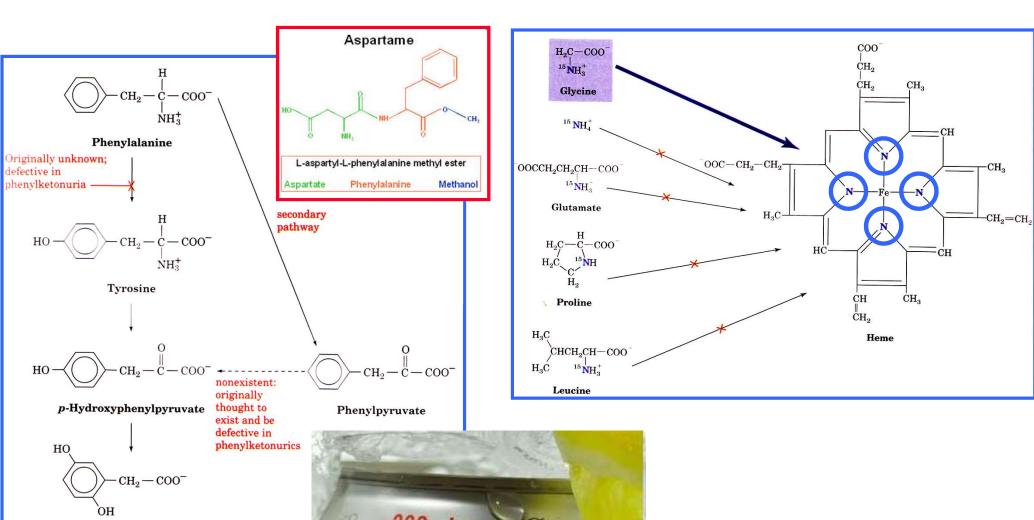
Modern Studies of Metabolism: Metabolomics



- Pathway intermediates accumulate:
- > upon genetic manipulation in transgenic animals/plants
- in the presence of metabolic inhibitors
- ➤ in the presence of genetic defects



Phenylketonuria and isotope labeling





Homogentisate

 $H_2O + CO_2$

Defective in alcaptonuria



02/07/22

ATP: The energizer of the cell

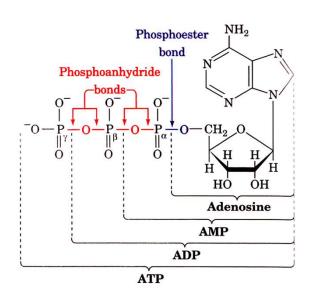
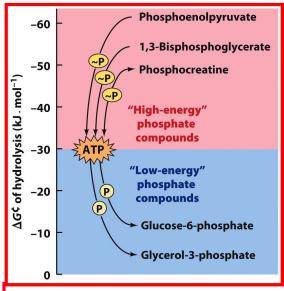


Table 16-3 Standard Free Energies of Phosphate Hydrolysis of Some Compounds of Biological Interest

Compound	$\Delta G^{\circ\prime}$ (kJ·mol ⁻¹)	
Compound		
Phosphoenolpyruvate	-61.9	
1,3-Bisphosphoglycerate	-49.4	
$ATP \left(\to AMP + PP_{i} \right)$	-45.6	
Acetyl phosphate	-43.1	
Phosphocreatine	-43.1	
ATP (\rightarrow ADP + P _i)	-30.5	
Glucose-1-phosphate	-20.9	
PP_i	-19.2	
Fructose-6-phosphate	-13.8	
Glucose-6-phosphate	-13.8	
Glycerol-3-phosphate	-9.2	

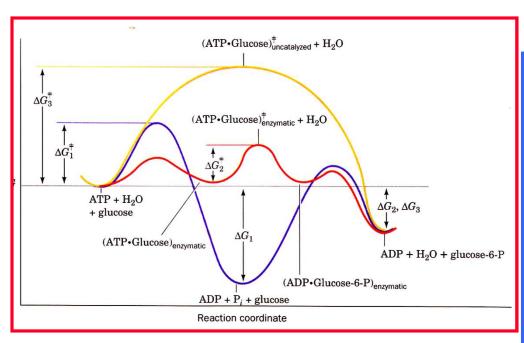
Source: Mostly from Jencks, W.P., in Fasman, G.D. (Ed.), Handbook of Biochemistry and Molecular Biology (3rd ed.), Physical and Chemical Data, Vol. I, pp. 296–304, CRC Press (1976).





(a)		$\Delta G^{\circ\prime} (kJ \cdot mol^{-1})$
Endergonic half-reaction 1	P_i + glucose -6-P + H_2O	+13.8
Exergonic half-reaction 2	$ATP \; + \; H_2O \qquad \qquad \Longrightarrow \; ADP \; + \; P_i$	-30.5
Overall coupled reaction	ATP + glucose \iff ADP + glucose-6-P	-16.7
(b) Exergonic half-reaction 1	$CH_2 = C$ $COO^ CH_2 = C$ $COO^ CH_2 = C$ $COO^ COO^ COO$	ΔG°' (kJ • mol [−] −61.9
	Phosphoenolpyruvate Pyruvate	
Endergonic half-reaction 2	ADP + $P_i \iff ATP + H_2O$	+30.5
Overall coupled reaction	$CH_2 = COO^-$ + ADP \iff $CH_3 - C - COO^-$ + ATP	-31.4

Balanced thermodynamics in life



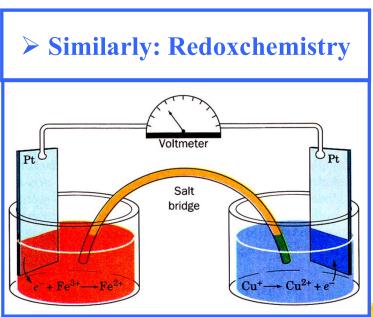


TABLE 16-4 Standard Reduction Potentials of Some Biochemically Important Half-reactions

Half-Reaction	&°′ (V)
$\frac{1}{2}O_2 + 2H^+ + 2e^- \Longrightarrow H_2O$	
$SO_4^{2-} + 2H^+ + 2e^- \Longrightarrow SO_3^{2-} + H_2O$	0.48
$NO_3^- + 2H^+ + 2e^- \Longrightarrow NO_2^- + H_2O$	0.42
Cytochrome a_3 (Fe ³⁺) + $e^- \rightleftharpoons$ cytochrome a_3 (Fe ²⁺)	0.385
$O_2(g) + 2H^+ + 2e^- \Longrightarrow H_2O_2$	0.295
Cytochrome a (Fe ³⁺) + $e^- \rightleftharpoons$ cytochrome a (Fe ²⁺)	0.29
Cytochrome c (Fe ³⁺) + $e^- \rightleftharpoons$ cytochrome c (Fe ²⁺)	0.235
Cytochrome c_1 (Fe ³⁺) + $e^- \rightleftharpoons$ cytochrome c_1 (Fe ²⁺)	0.22
Cytochrome b (Fe ³⁺) + $e^- \rightleftharpoons$ cytochrome b (Fe ²⁺) (mitochondrial)	0.077
Ubiquinone $+ 2H^+ + 2e^- \Longrightarrow$ ubiquinol	0.045
Fumarate ⁻ + $2H^+ + 2e^- \iff$ succinate ⁻	0.031
$FAD + 2H^+ + 2e^- \Longrightarrow FADH_2$ (in flavoproteins)	-0.040
Oxaloacetate ⁻ + $2H^+$ + $2e^- \Longrightarrow malate^-$	-0.166
Pyruvate ⁻ + $2H^+ + 2e^- \iff$ lactate ⁻	-0.185
Acetaldehyde + $2H^+ + 2e^- \rightleftharpoons$ ethanol	
$FAD + 2H^+ + 2e^- \Longrightarrow FADH_2$ (free coenzyme)	
$S + 2H^+ + 2e^- \Longrightarrow H_2S$	
Lipoic acid $+2H^+ + 2e^- \iff$ dihydrolipoic acid	
$NAD^+ + H^+ + 2e^- \Longrightarrow NADH$	
$NADP^{+} + H^{+} + 2e^{-} \Longrightarrow NADPH$	-0.320
Cystine $+ 2H^+ + 2e^- \Longrightarrow 2$ cysteine	-0.340
Acetoacetate ⁻ + $2H^+$ + $2e^- \iff \beta$ -hydroxybutyrate ⁻	
$\mathrm{H}^+ + e^- \Longrightarrow \frac{1}{2}\mathrm{H}_2$	
Acetate ⁻ + $3H^+$ + $2e^ \Longrightarrow$ acetaldehyde + H_2O	-0.581

Source: Mostly from Loach, P.A., in Fasman, G.D. (Ed.), Handbook of Biochemistry and Molecular Biology (3rd ed.), Physical and Chemical Data, Vol. I, pp. 123–130, CRC Press (1976).

Nils Walter: Chem 4

Chapter 16: What have we learned?

- **Wetabolism: Complex food processing**
- **Types of chemistries in metabolism**

Wetabolomics



Energy metabolism: ATP and the flow of phosphoryl groups

© Redox metabolism: NAD+, FAD and the flow of electrons