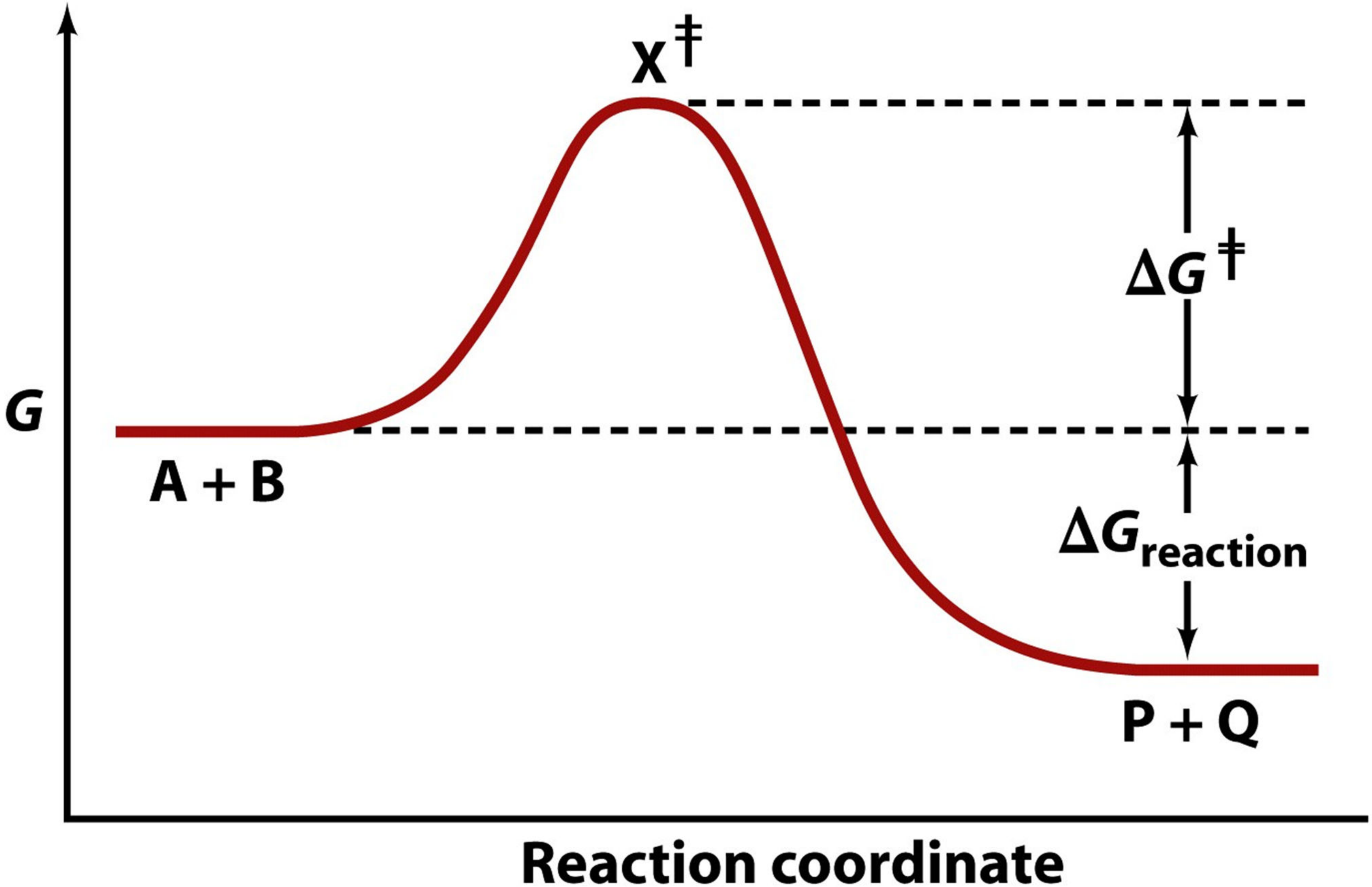
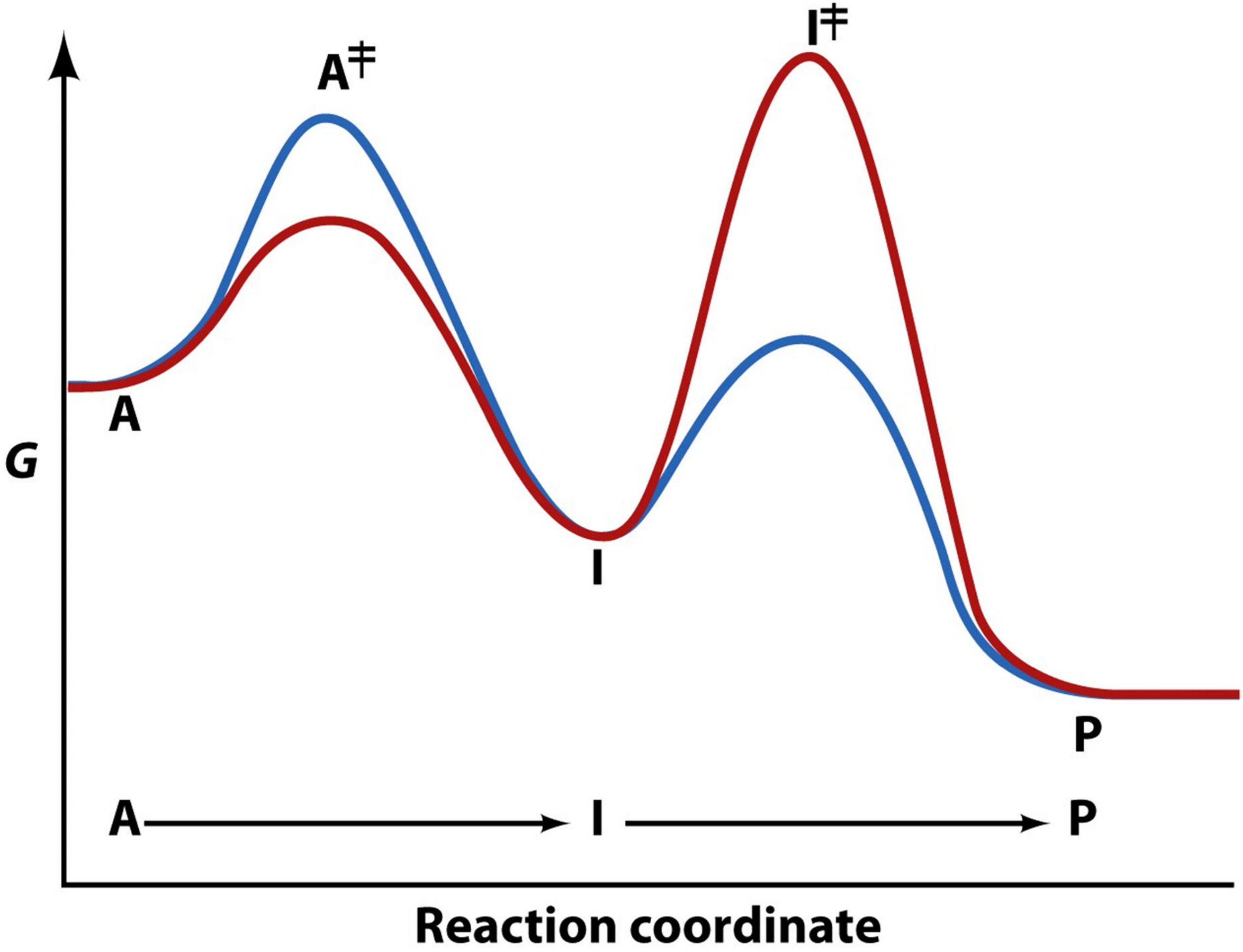

$X^{\ddagger}$
G
$\Delta G^{\ddagger}$
A + B
$\Delta G_{\text{reaction}}$
P + Q
Reaction coordinate


A‡
I‡
G
A
I
P
A → I → P
Reaction coordinate

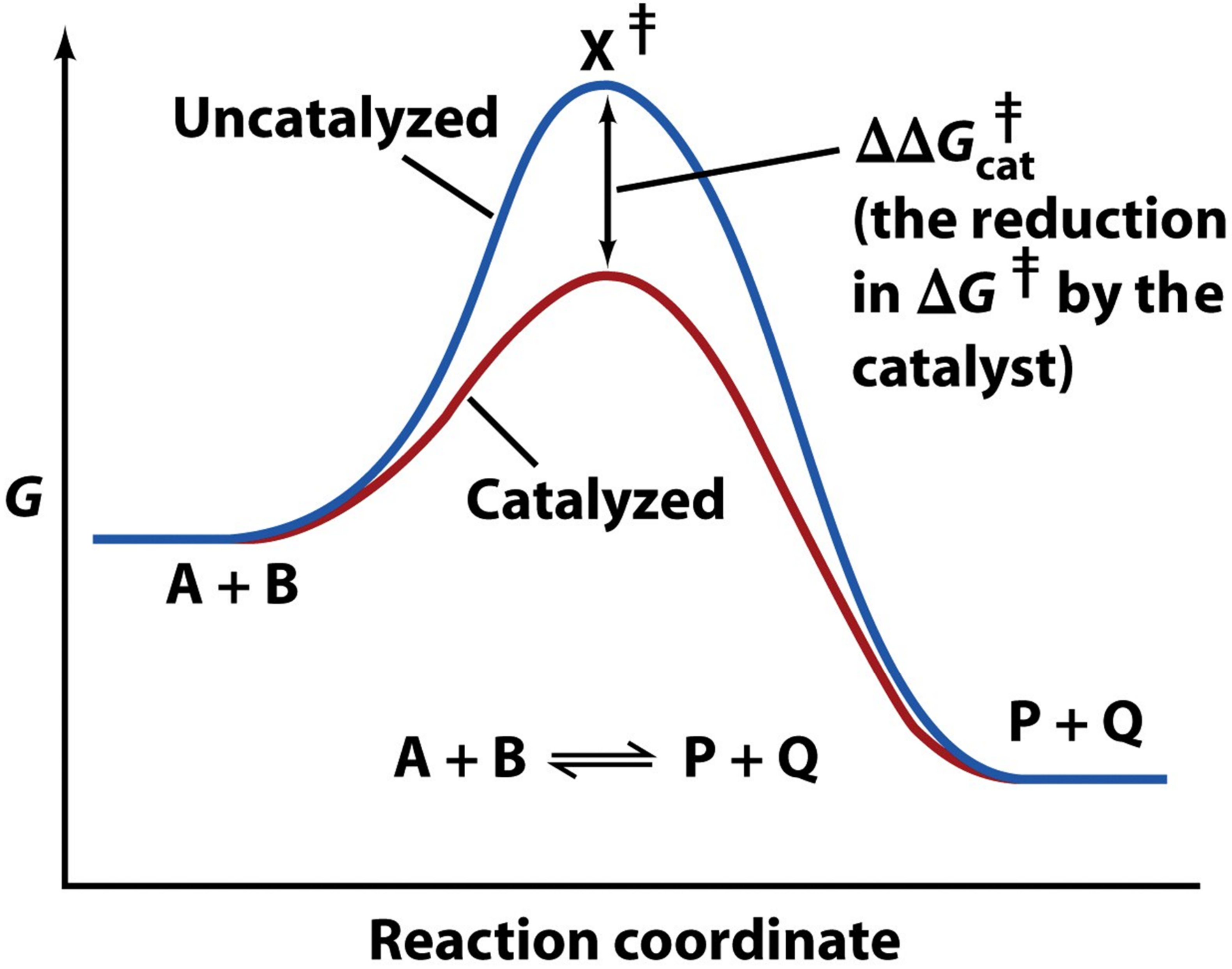

X‡
Uncatalyzed
$\Delta\Delta G^{\ddagger}_{cat}$
(the reduction in $\Delta G^{\ddagger}$ by the catalyst)
G
Catalyzed
A + B
P + Q
$A + B \rightleftharpoons P + Q$
Reaction coordinate

Table 11-2 Enzyme Classification According to Reaction Type

Classification	Type of Reaction Catalyzed
1. Oxidoreductases	Oxidation–reduction reactions
2. Transferases	Transfer of functional groups
3. Hydrolases	Hydrolysis reactions
4. Lyases	Group elimination to form double bonds
5. Isomerases	Isomerization
6. Ligases	Bond formation coupled with ATP hydrolysis

Pyruvate is reduced to lactate in anaerobic metabolism in muscle cells

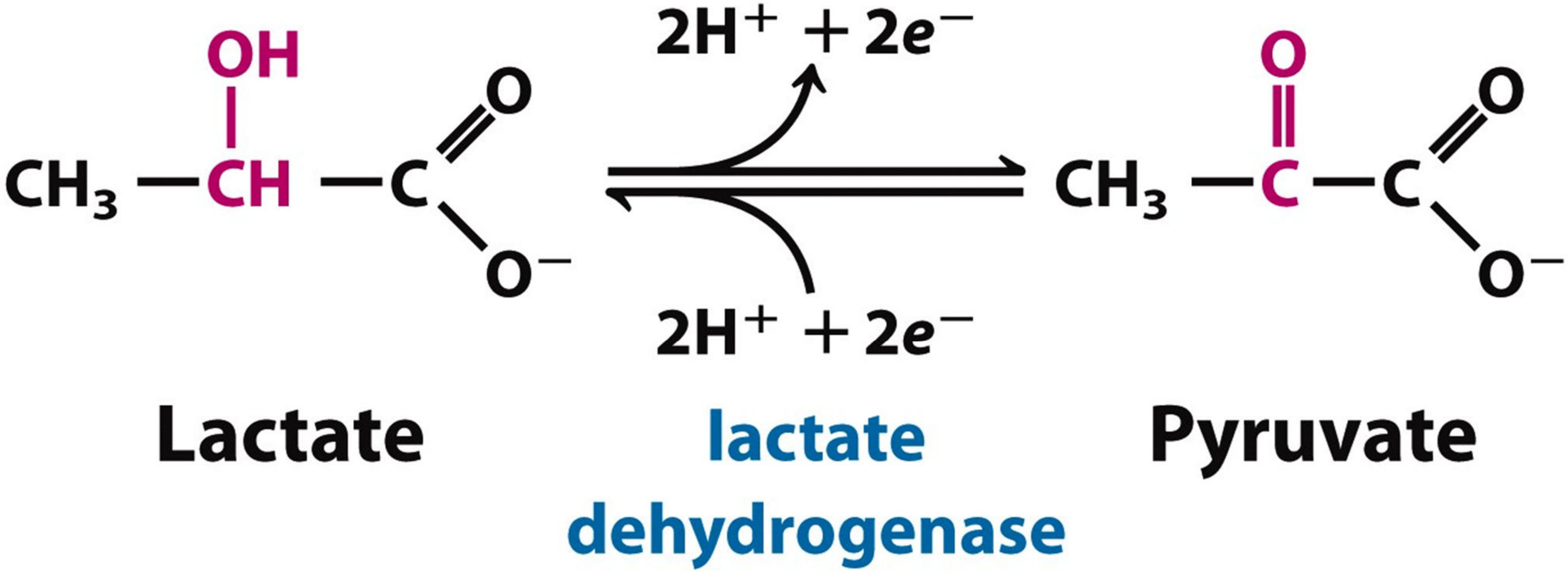


Figure 13-10
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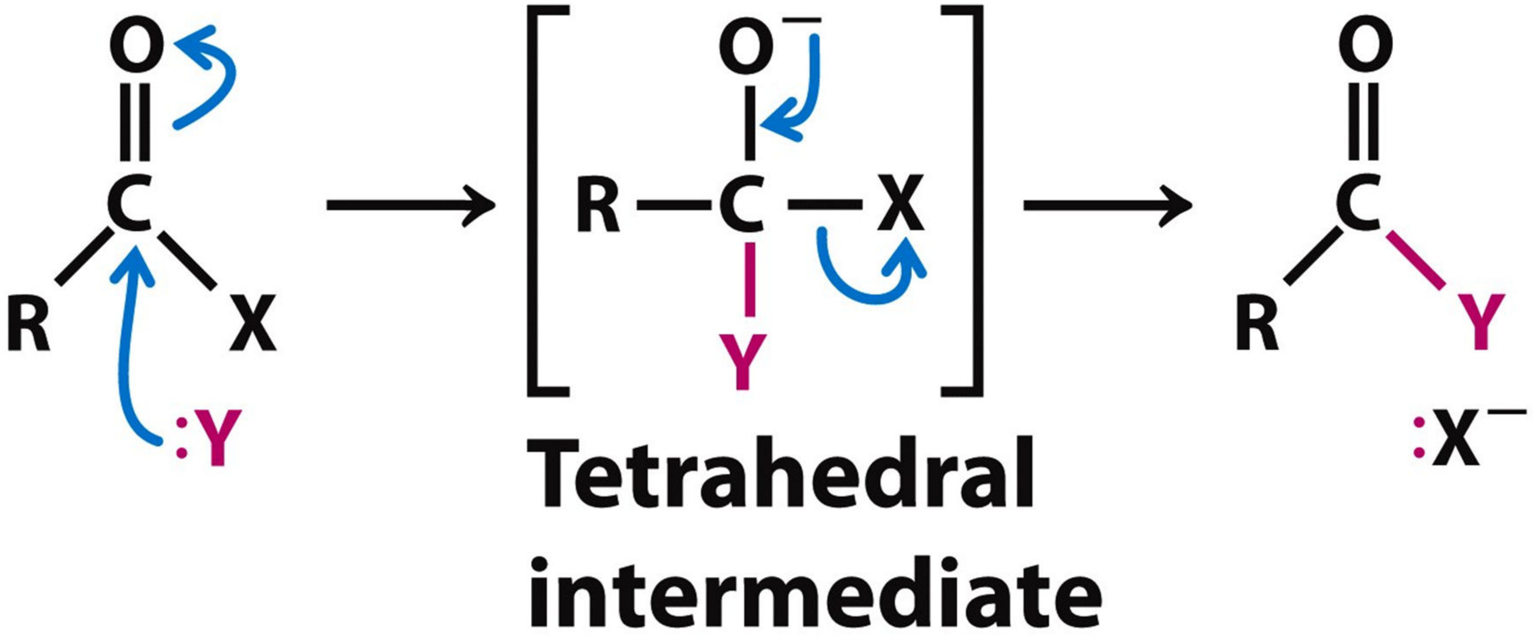
Transferases and hydrolases catalyze group transfer reactions

Acyl transfer:



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Hexokinase catalyzes a phosphoryl transfer from ATP to glucose

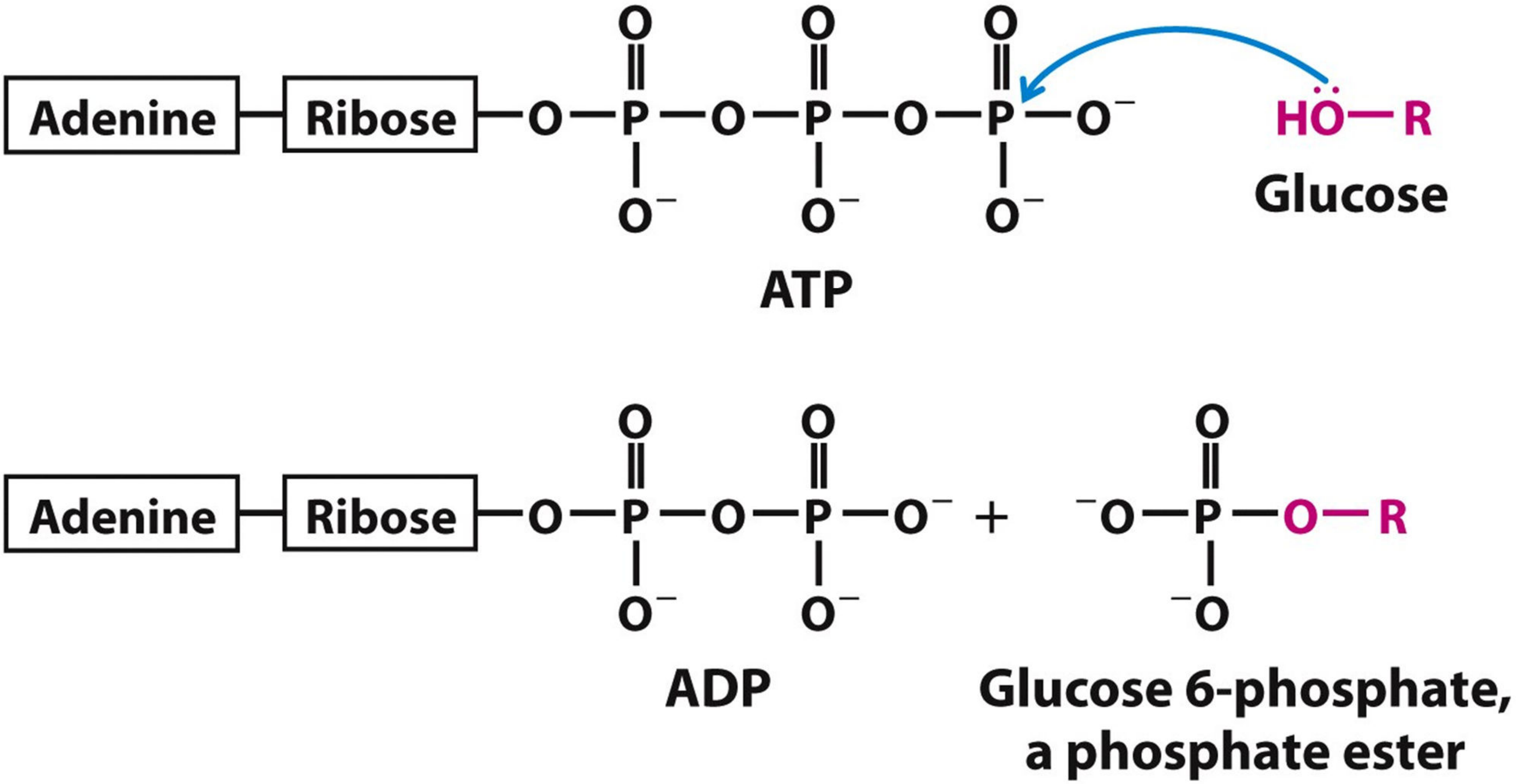

Figure 13-8c

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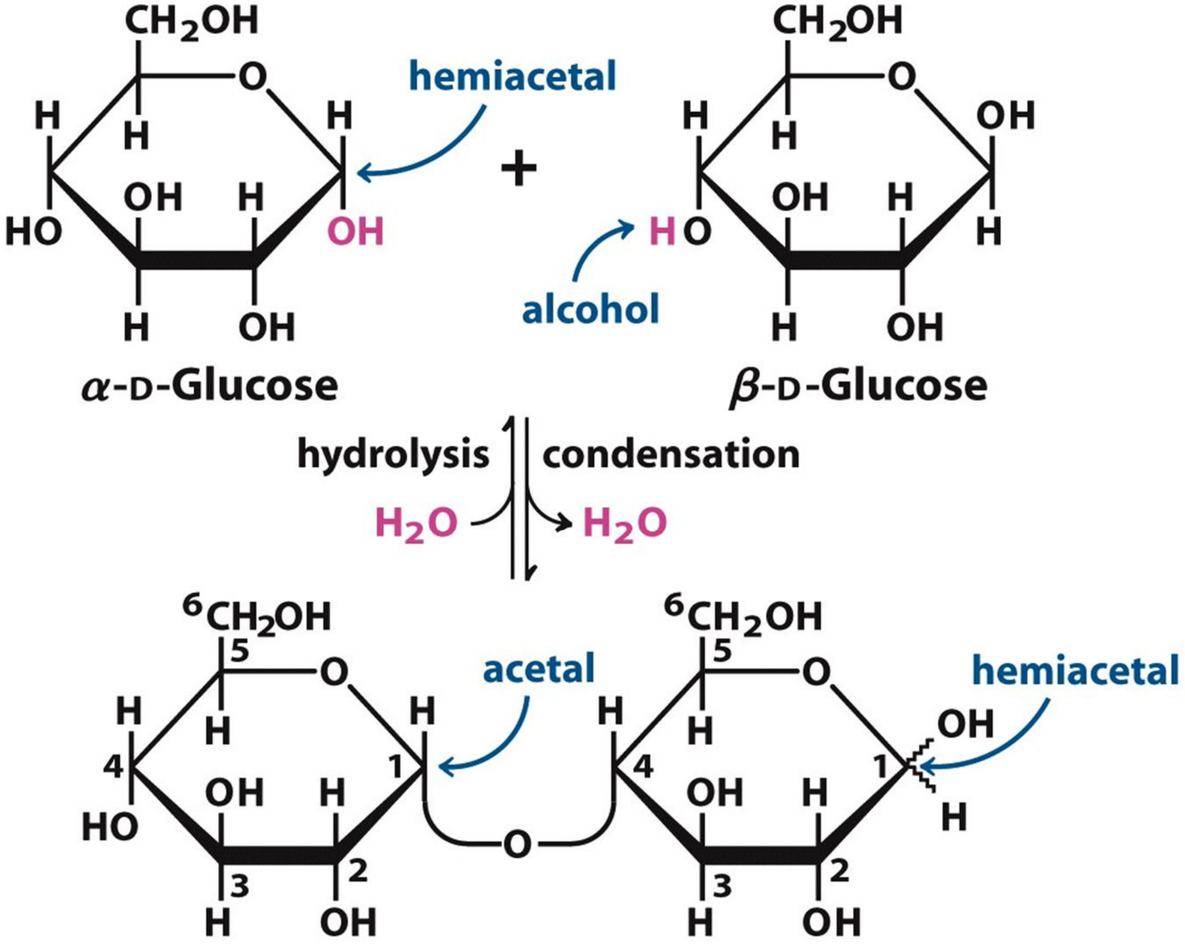
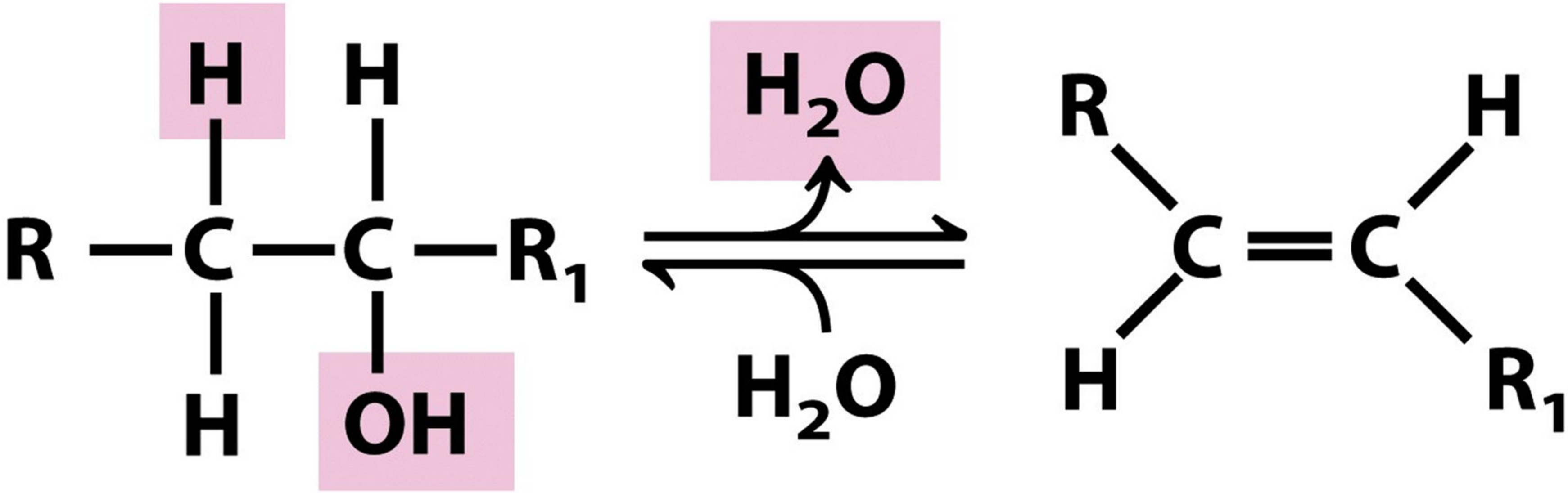
Glycosidases are hydrolases, catalyzing hydrolysis of glycosidic bonds



Maltose

α-D-glucopyranosyl-(1→4)-D-glucopyranose

Lyases catalyze eliminations and the formation/breaking of carbon-carbon bonds



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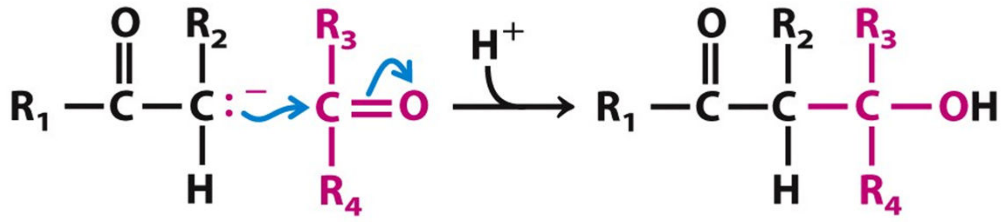
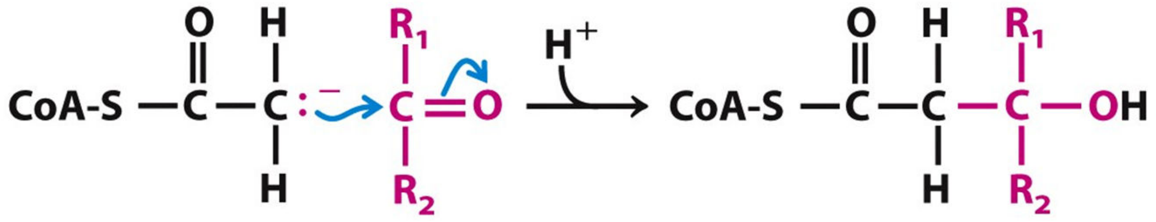
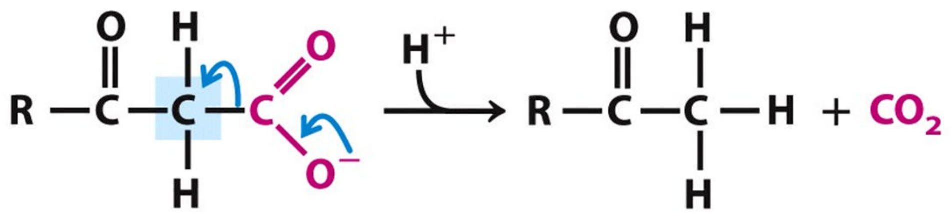
Lyases catalyze eliminations and the formation/breaking of carbon-carbon bonds



Aldol condensation



Claisen ester condensation



Decarboxylation of a β-keto acid

Figure 13-4
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Isomerases catalyze isomerizations or internal rearrangements

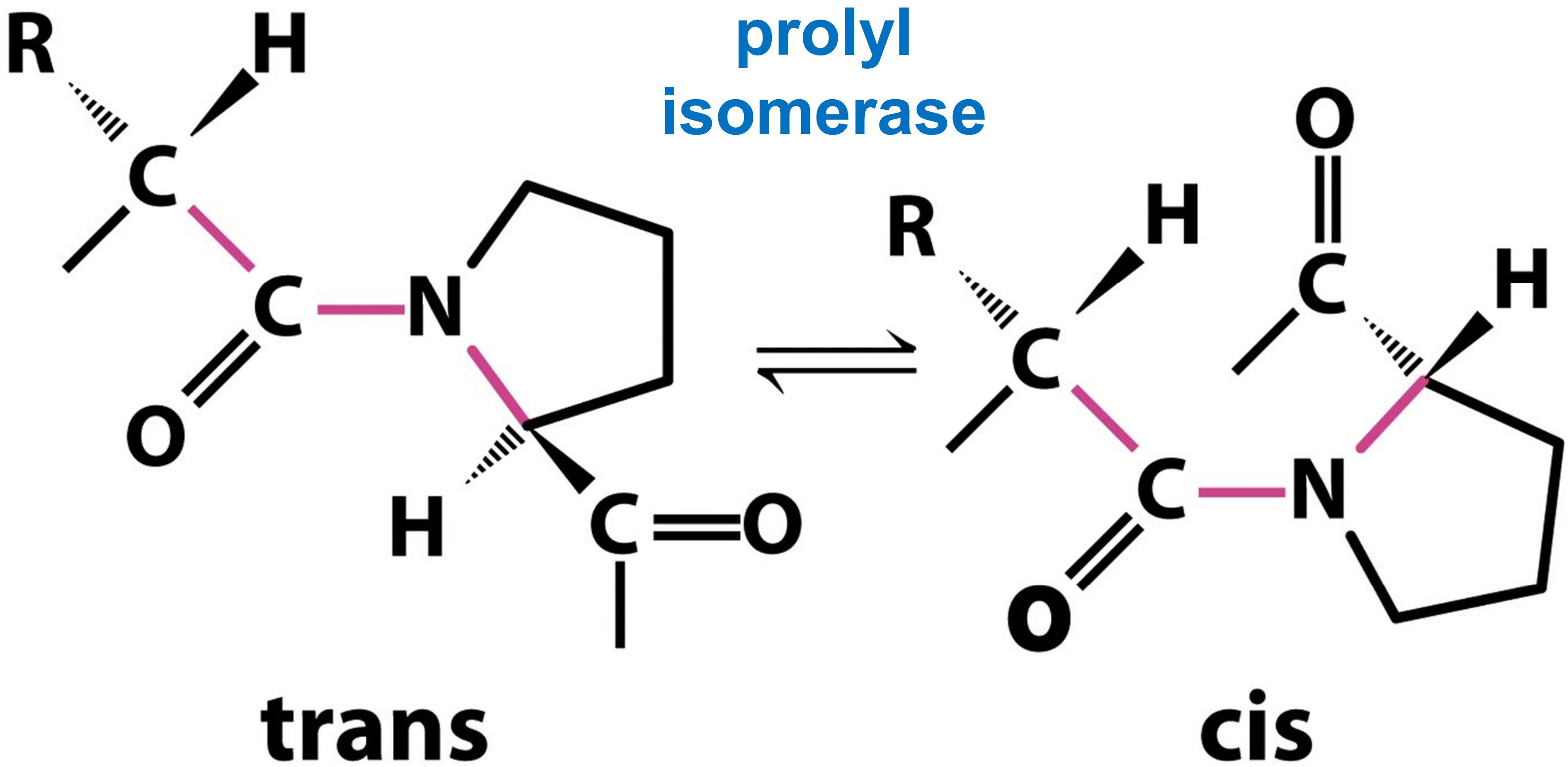

Figure 4-7b
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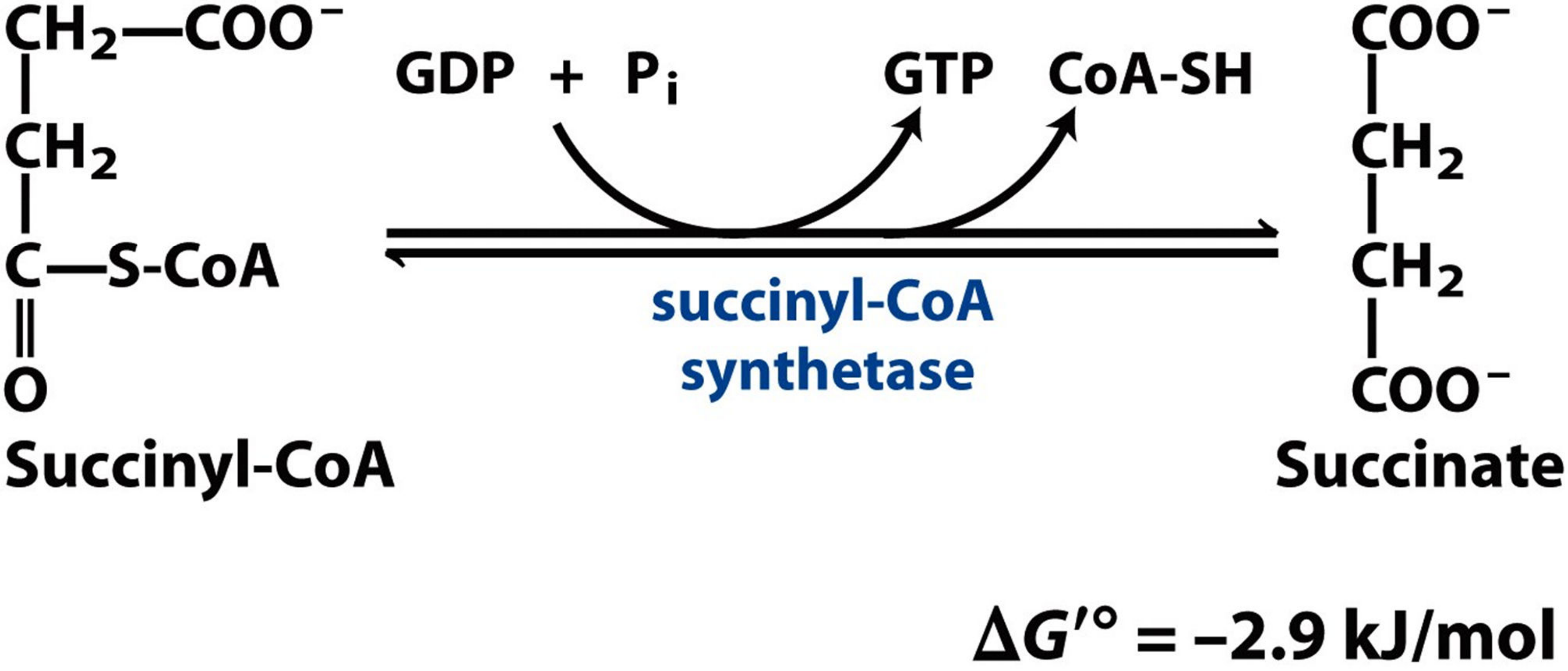
Ligases couple ATP (or NTP) hydrolysis with bond formation



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Enzymes can dramatically enhance reaction rates

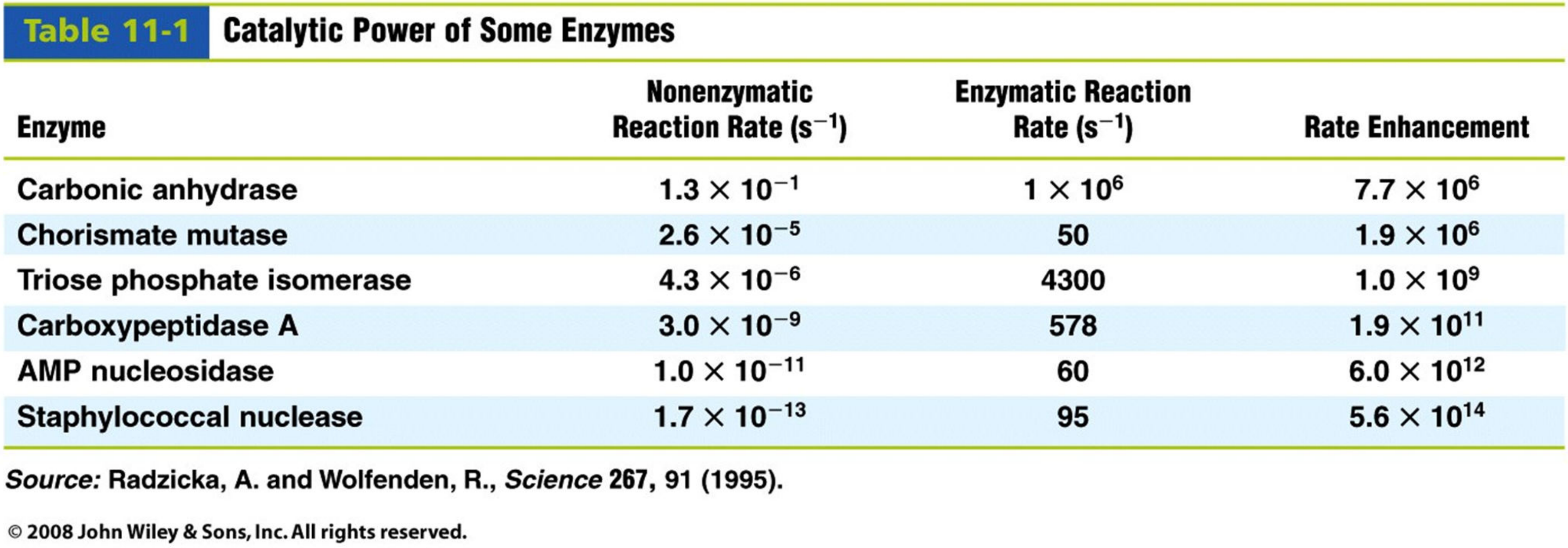


Table 11-1 **Catalytic Power of Some Enzymes**

Enzyme	Nonenzymatic Reaction Rate (s^{-1})	Enzymatic Reaction Rate (s^{-1})	Rate Enhancement
Carbonic anhydrase	1.3×10^{-1}	1×10^{6}	7.7×10^{6}
Chorismate mutase	2.6×10^{-5}	50	1.9×10^{6}
Triose phosphate isomerase	4.3×10^{-6}	4300	1.0×10^{9}
Carboxypeptidase A	3.0×10^{-9}	578	1.9×10^{11}
AMP nucleosidase	1.0×10^{-11}	60	6.0×10^{12}
Staphylococcal nuclease	1.7×10^{-13}	95	5.6×10^{14}

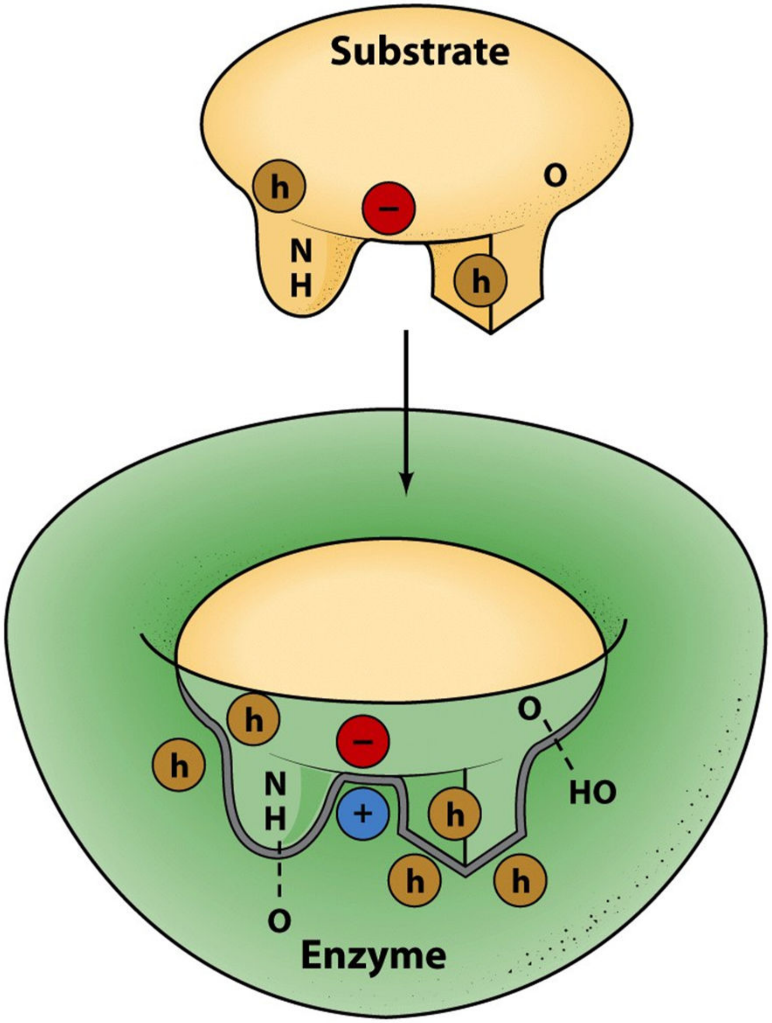
Source: Radzicka, A. and Wolfenden, R., *Science* **267**, 91 (1995).

How do they do it?

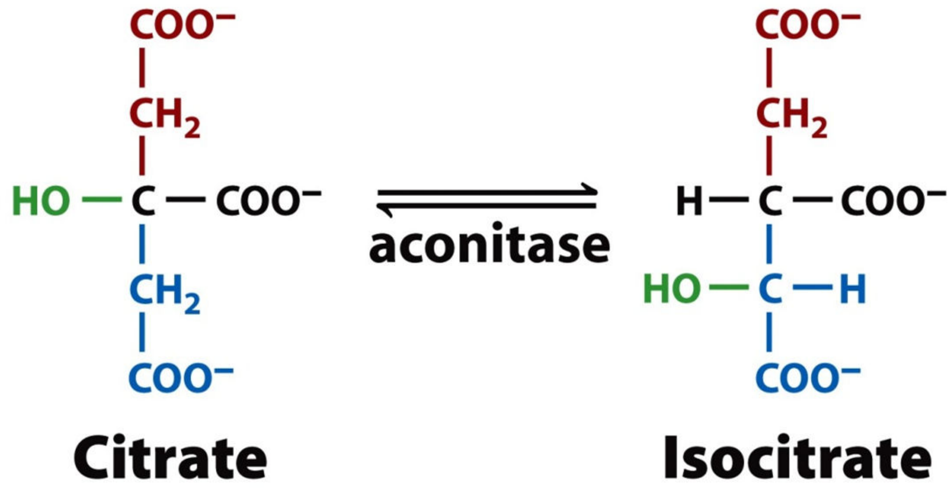
Enzymes use several catalytic mechanisms (often together) to enhance reaction rates

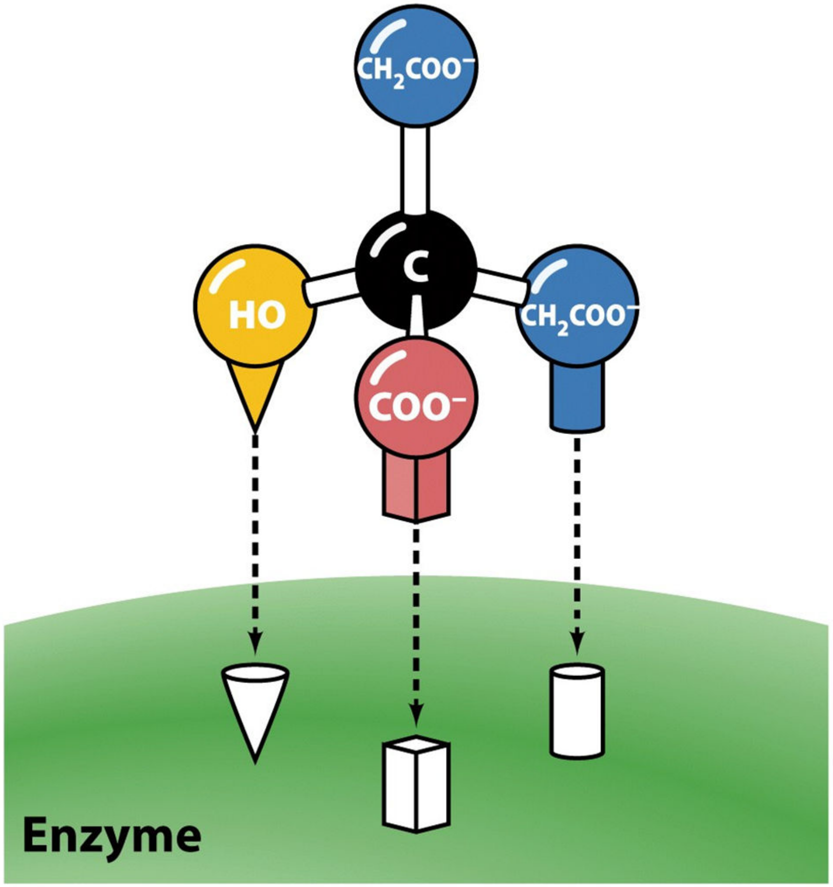
- Proximity and orientation effects: the enzyme specifically binds and positions substrates (with respect to each other and to enzyme functional groups) to maximize reactivity
- Electrostatic catalysis: the enzyme uses charge-charge interactions in catalysis
- Preferential binding of transition state: binding interactions between the enzyme and TS are maximized; they are greater than those in the enzyme-substrate or enzyme-product complexes
- General acid and general base catalysis: functional groups of the enzyme donate &/or accept protons
- Covalent catalysis: the enzyme forms a covalent bond with the substrate
- Metal-ion catalysis: the enzyme uses a metal ion to aid catalysis

Enzymes bind their substrates with geometric and electronic complementarity

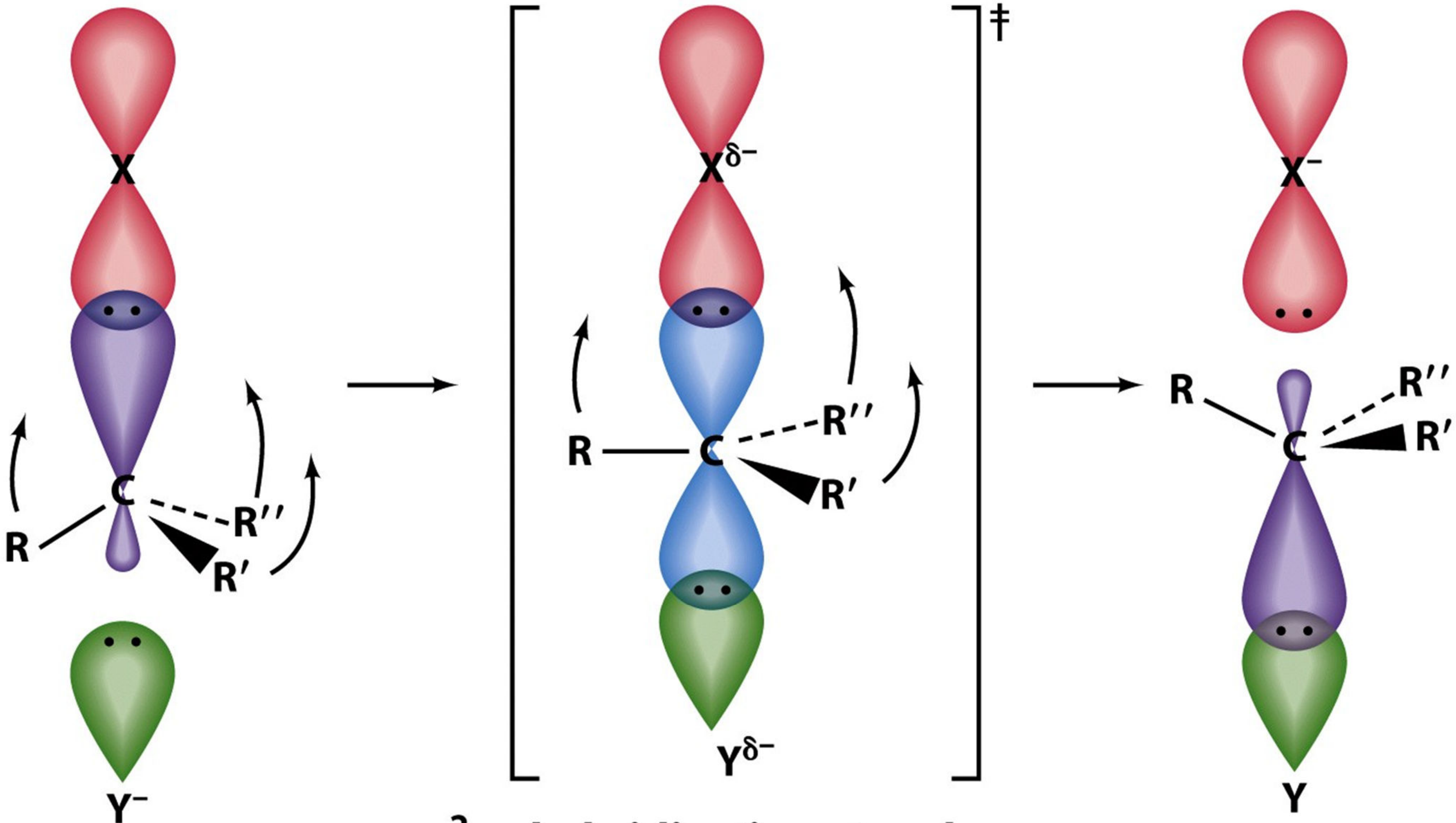


Enzymes are stereoselective (ex: aconitase)





Binding complementarity positions substrates to maximize reaction rates



***sp*²–*p* hybridization at carbon**

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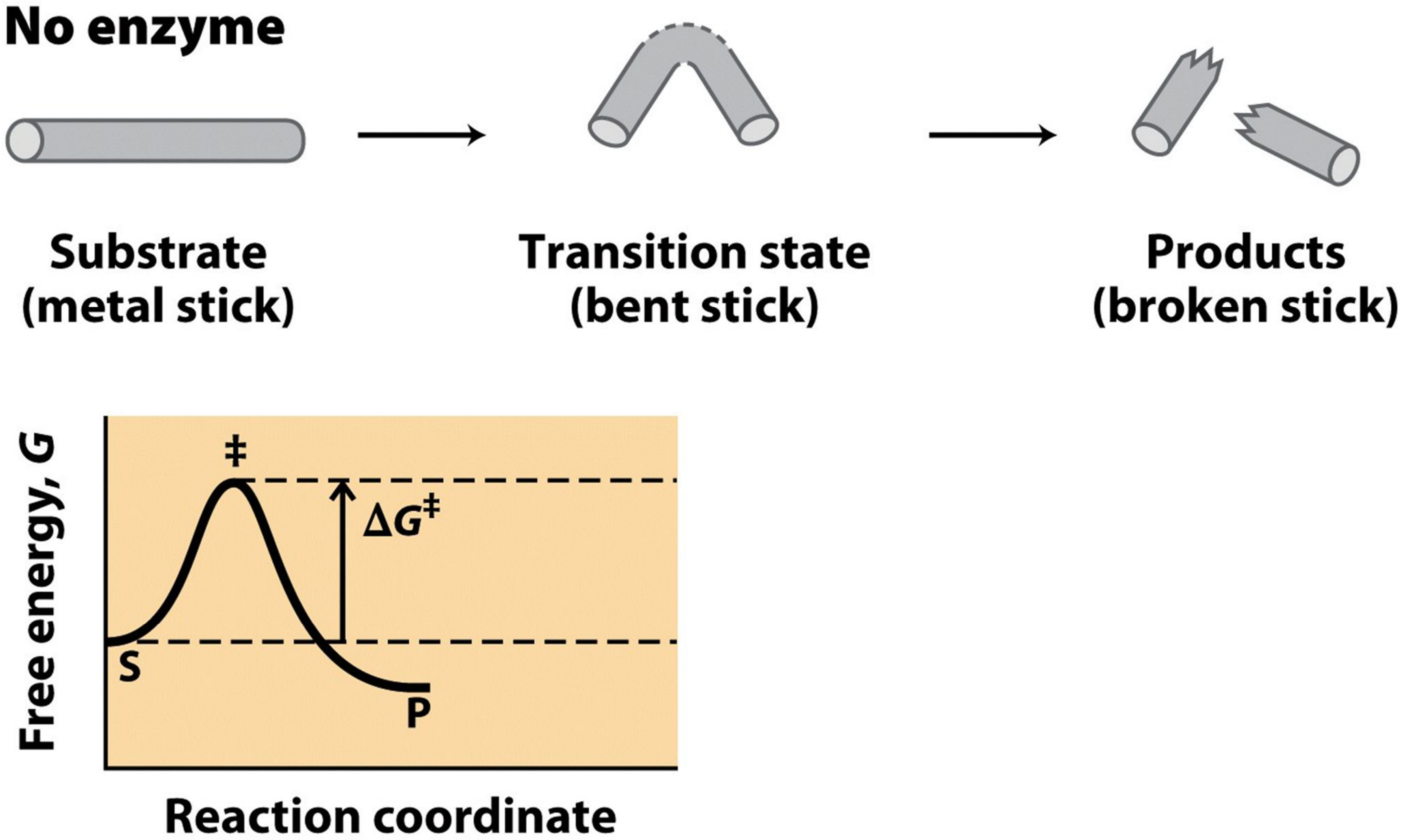

Figure 6-5a
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Enzyme complementary to substrate

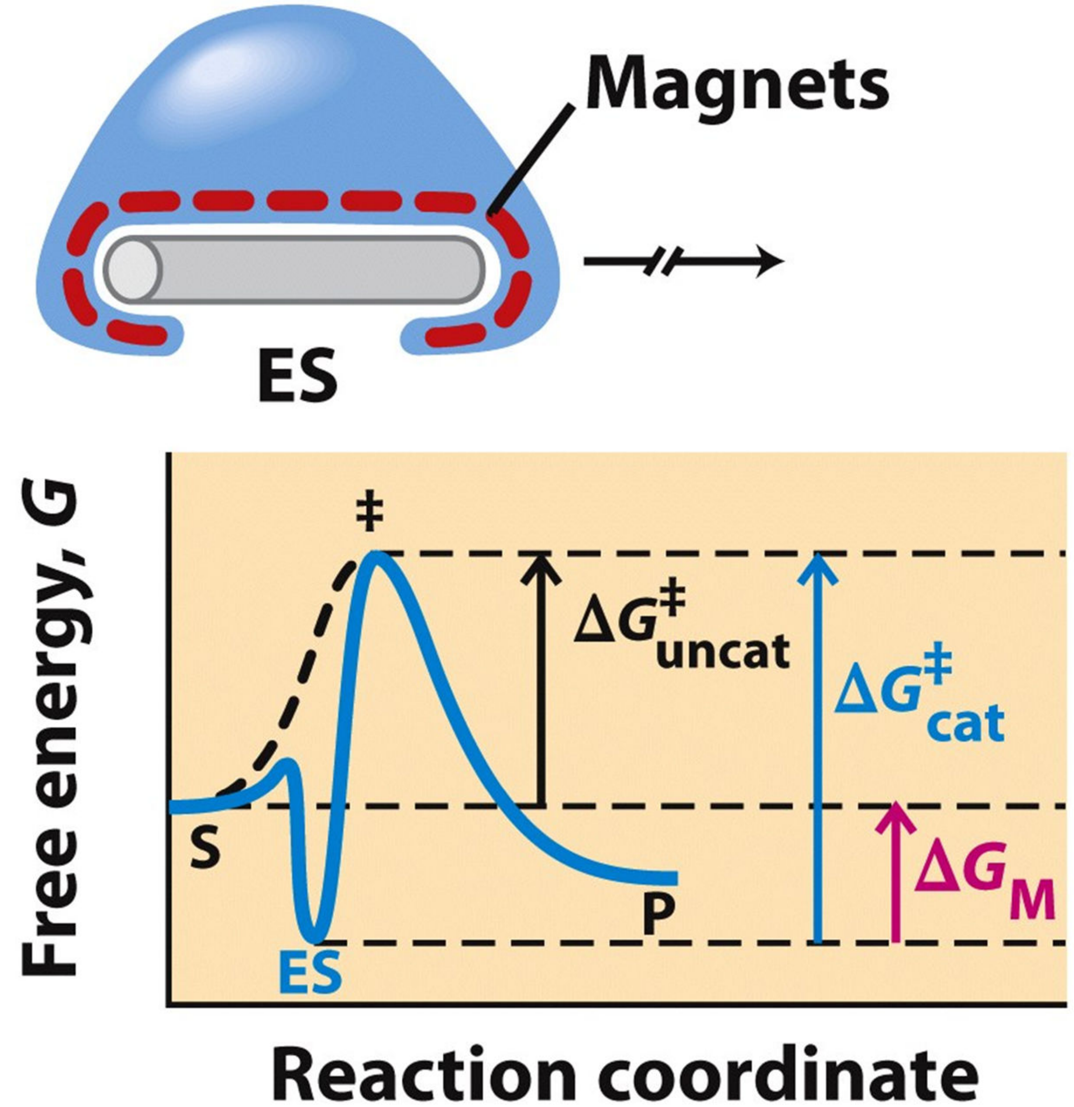

Figure 6-5b

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Enzyme complementary to transition state

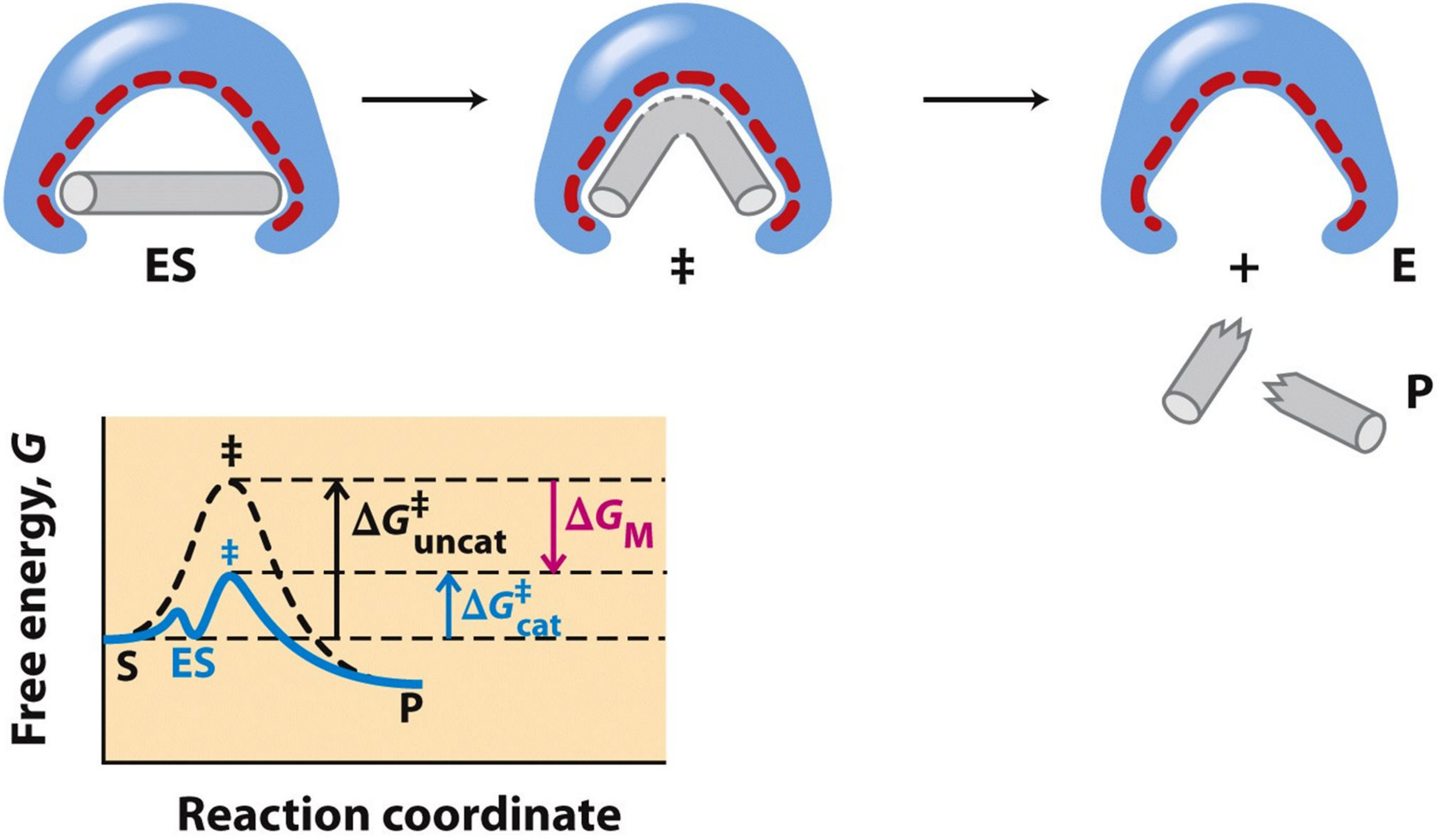

Figure 6-5c

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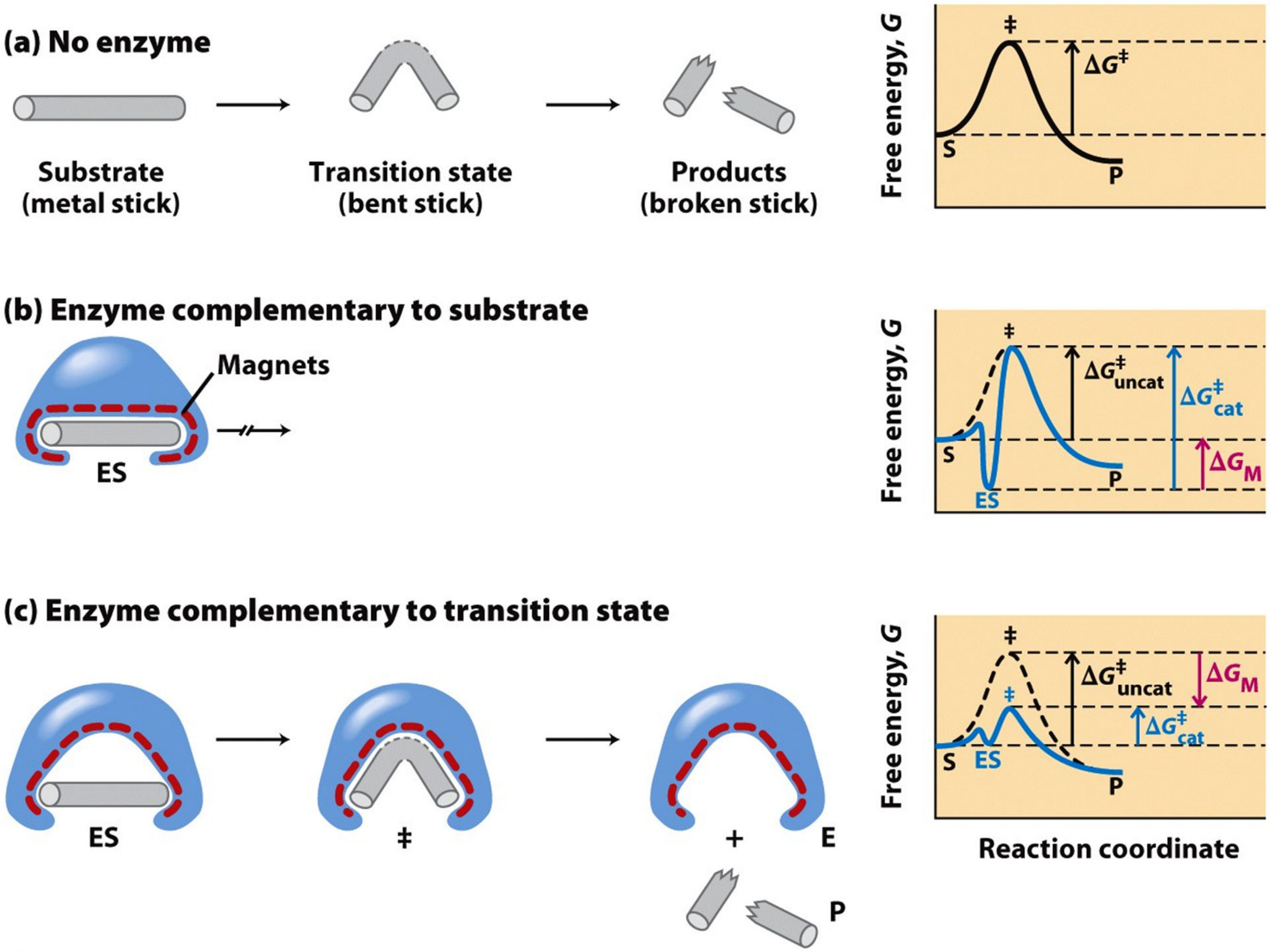

Figure 6-5

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Enzymes use several catalytic mechanisms (often together) to enhance reaction rates

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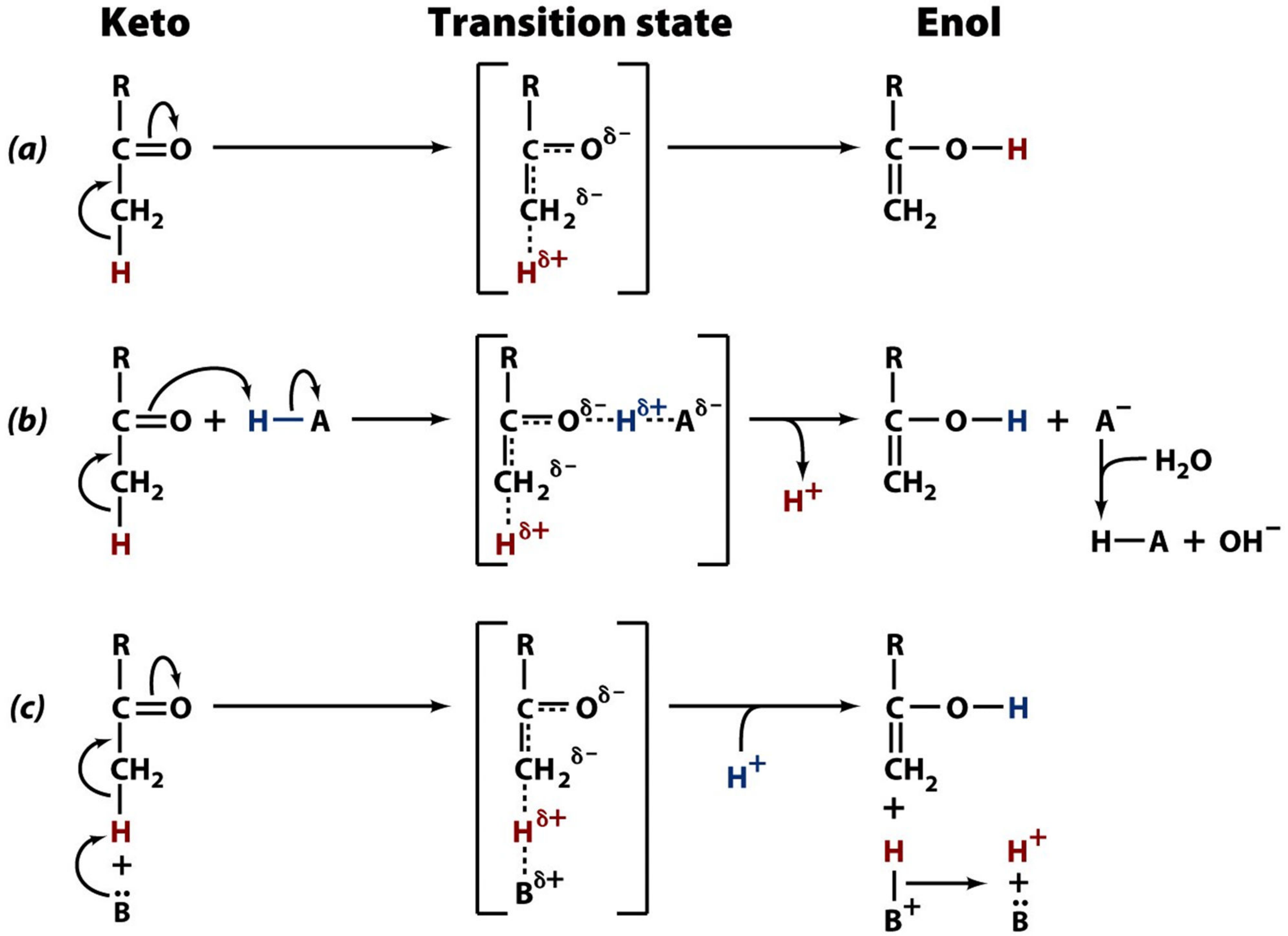
- General acid and general base catalysis: functional groups of the enzyme donate &/or accept protons
- Covalent catalysis: the enzyme forms a covalent bond with the substrate
- Metal-ion catalysis: the enzyme uses a metal ion to aid catalysis


Keto
Transition state
Enol
(a)
(b)
(c)
R
C
O
CH_2
H
$O^{\delta-}$
$CH_2^{\delta-}$
$H^{\delta+}$
C—O—H
CH_2
H—A
$O^{\delta-}$···$H^{\delta+}$···$A^{\delta-}$
H^+
A^-
H_2O
H—A + OH^-
B
$B^{\delta+}$
B^+

Enzymes use several catalytic mechanisms (often together) to enhance reaction rates

- Proximity and orientation effects: the enzyme specifically binds and positions substrates (with respect to each other and to enzyme functional groups) to maximize reactivity
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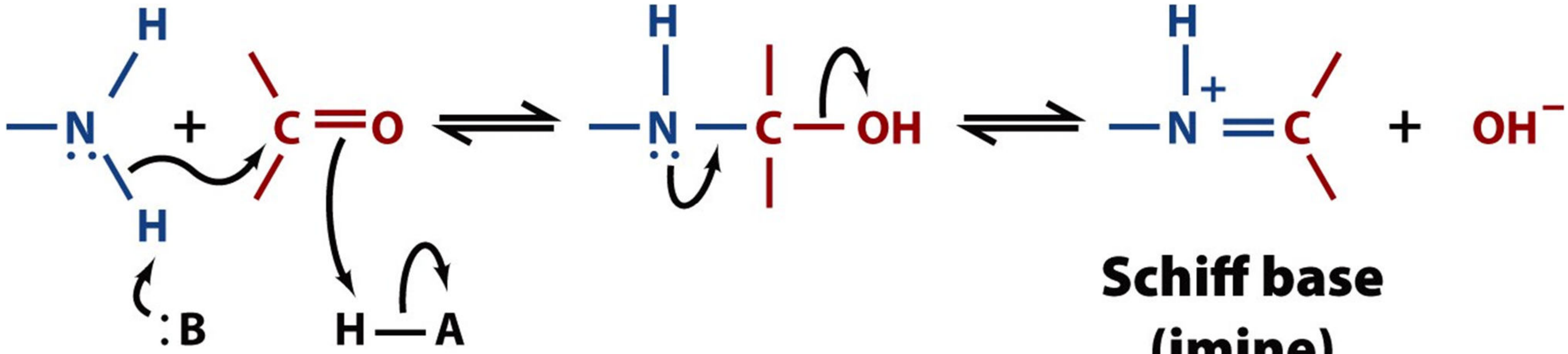
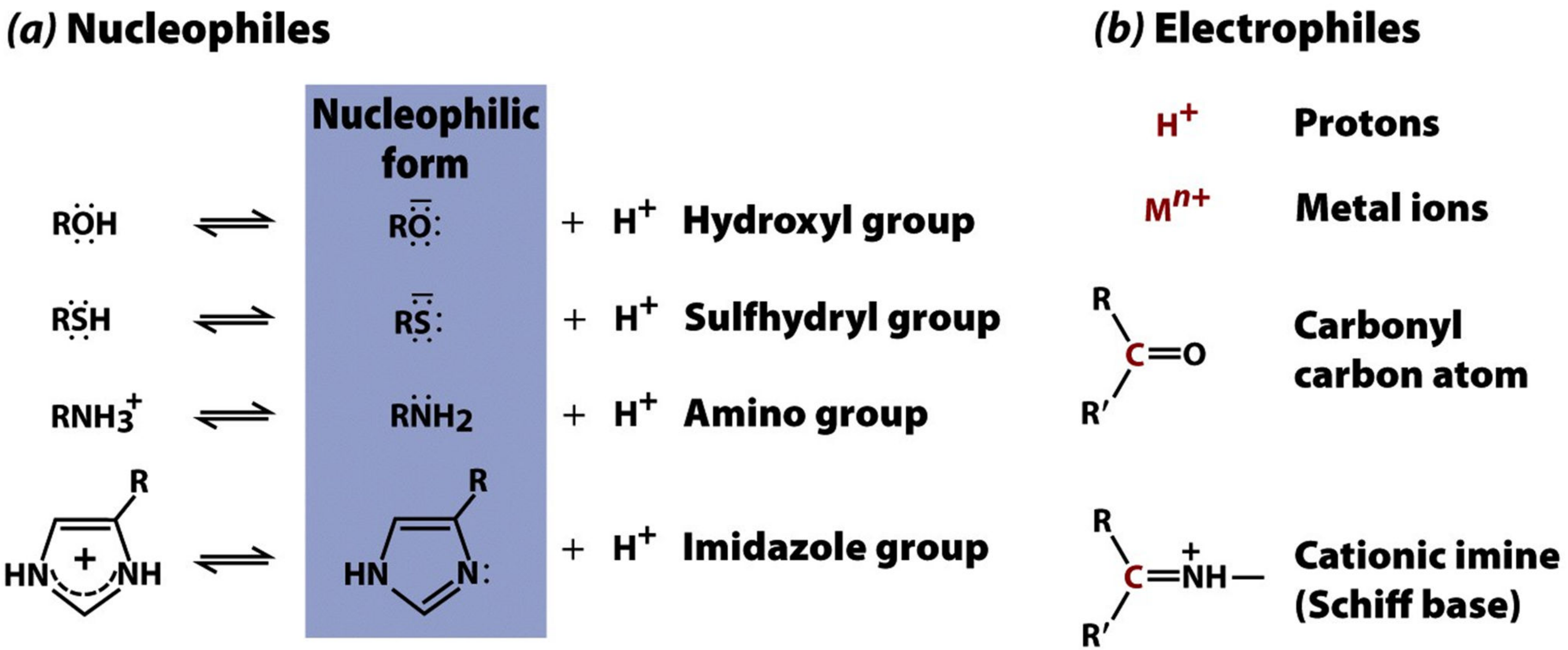


Schiff base
(imine)

Acid-base and covalent catalysis rely on nucleophile-electrophile chemistry



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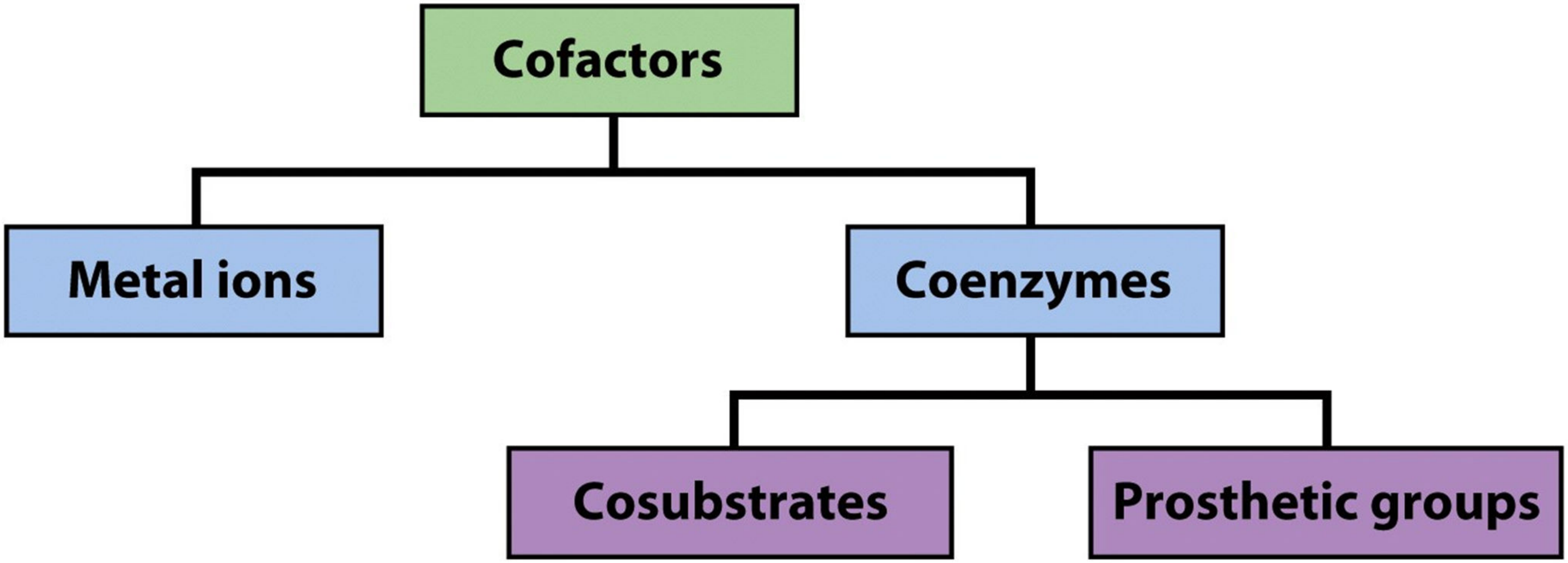
- Covalent catalysis: the enzyme forms a covalent bond with the substrate
- Metal-ion catalysis: the enzyme uses a metal ion to aid catalysis

Proteins use cofactors to expand their range of functions



- Cofactors
  - Metal ions
  - Coenzymes
    - Cosubstrates
    - Prosthetic groups

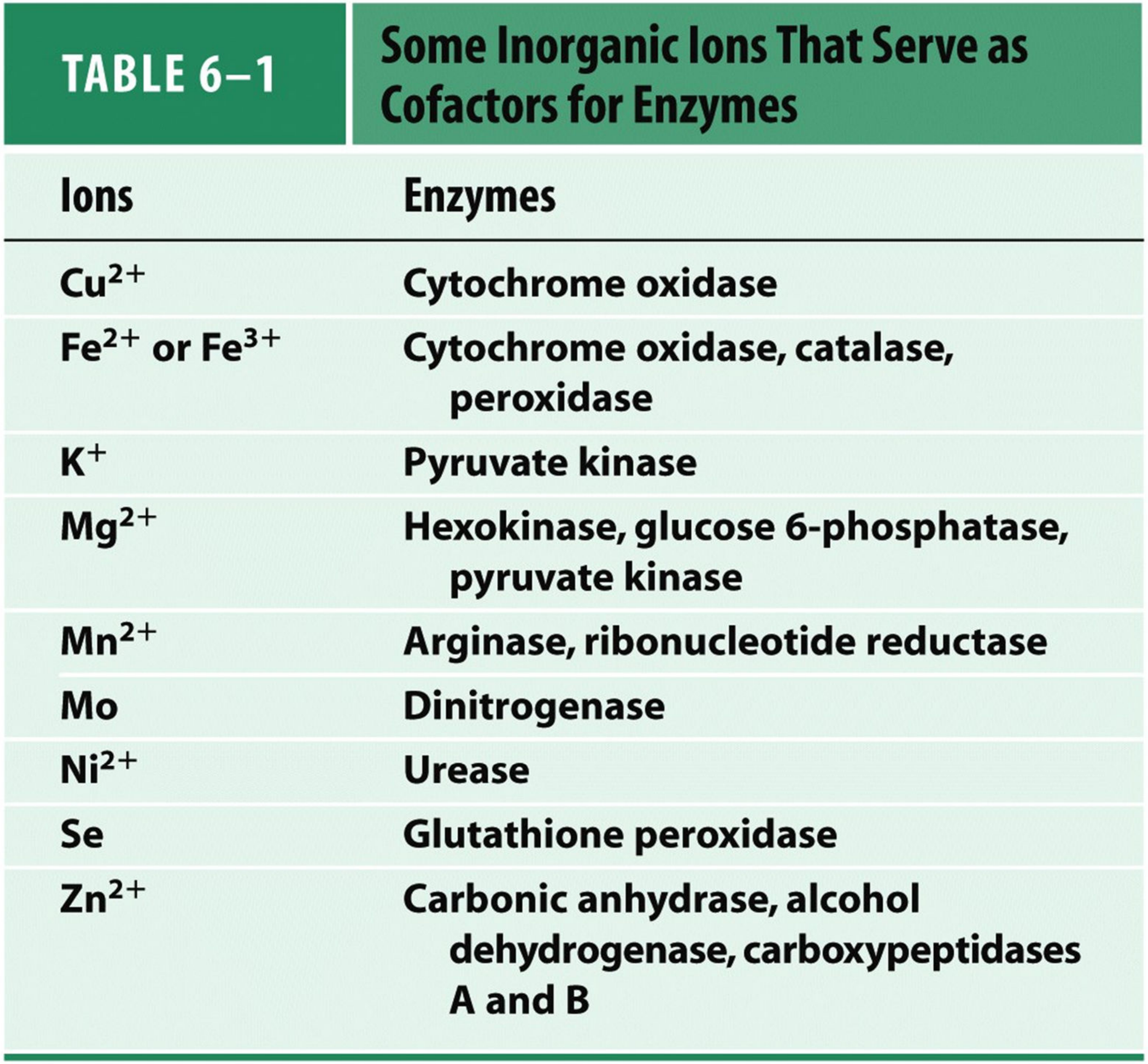


TABLE 6–1 Some Inorganic Ions That Serve as Cofactors for Enzymes

Ions	Enzymes
Cu^{2+}	Cytochrome oxidase
Fe^{2+} or Fe^{3+}	Cytochrome oxidase, catalase, peroxidase
K^{+}	Pyruvate kinase
Mg^{2+}	Hexokinase, glucose 6-phosphatase, pyruvate kinase
Mn^{2+}	Arginase, ribonucleotide reductase
Mo	Dinitrogenase
Ni^{2+}	Urease
Se	Glutathione peroxidase
Zn^{2+}	Carbonic anhydrase, alcohol dehydrogenase, carboxypeptidases A and B

Table 6-1
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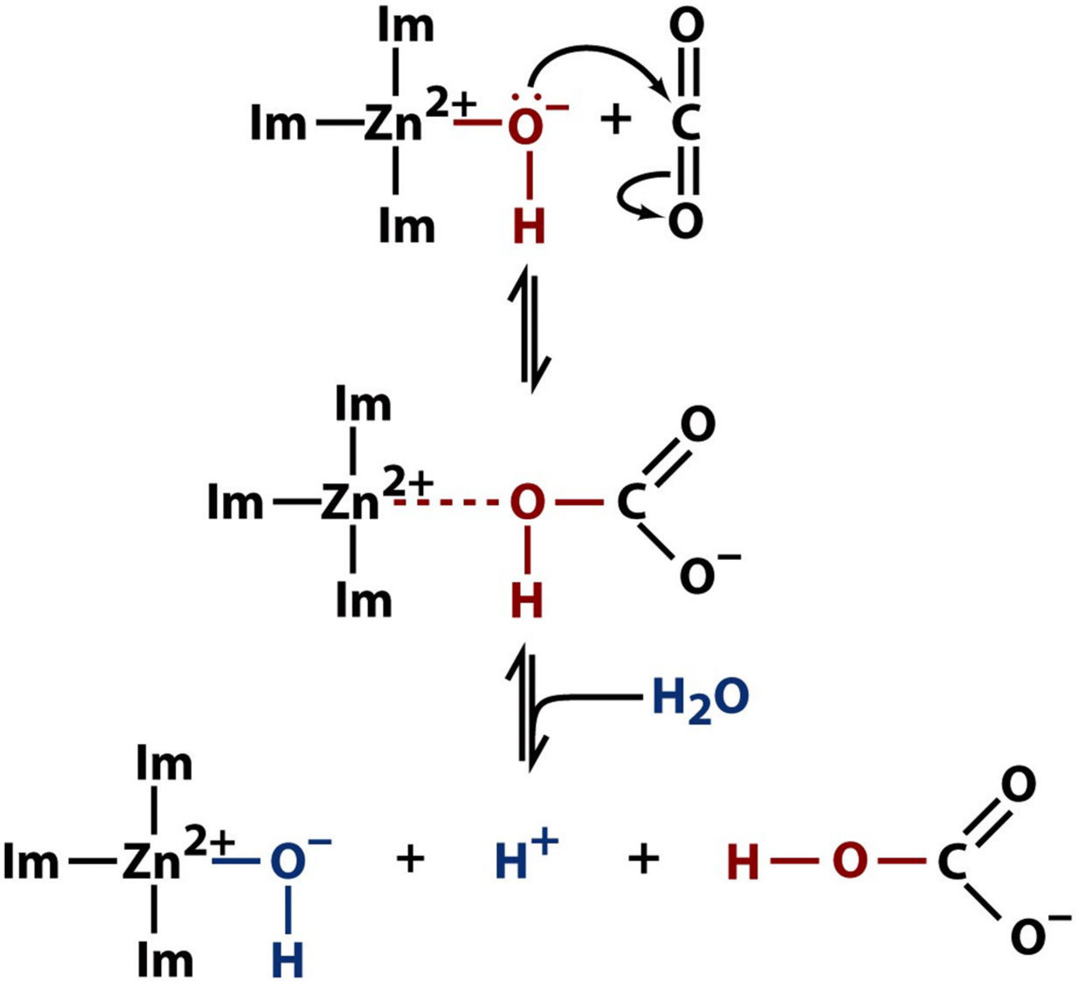
Carbonic anhydrase uses Zn^{2+} for catalysis



Enzymes use several catalytic mechanisms (often together) to enhance reaction rates

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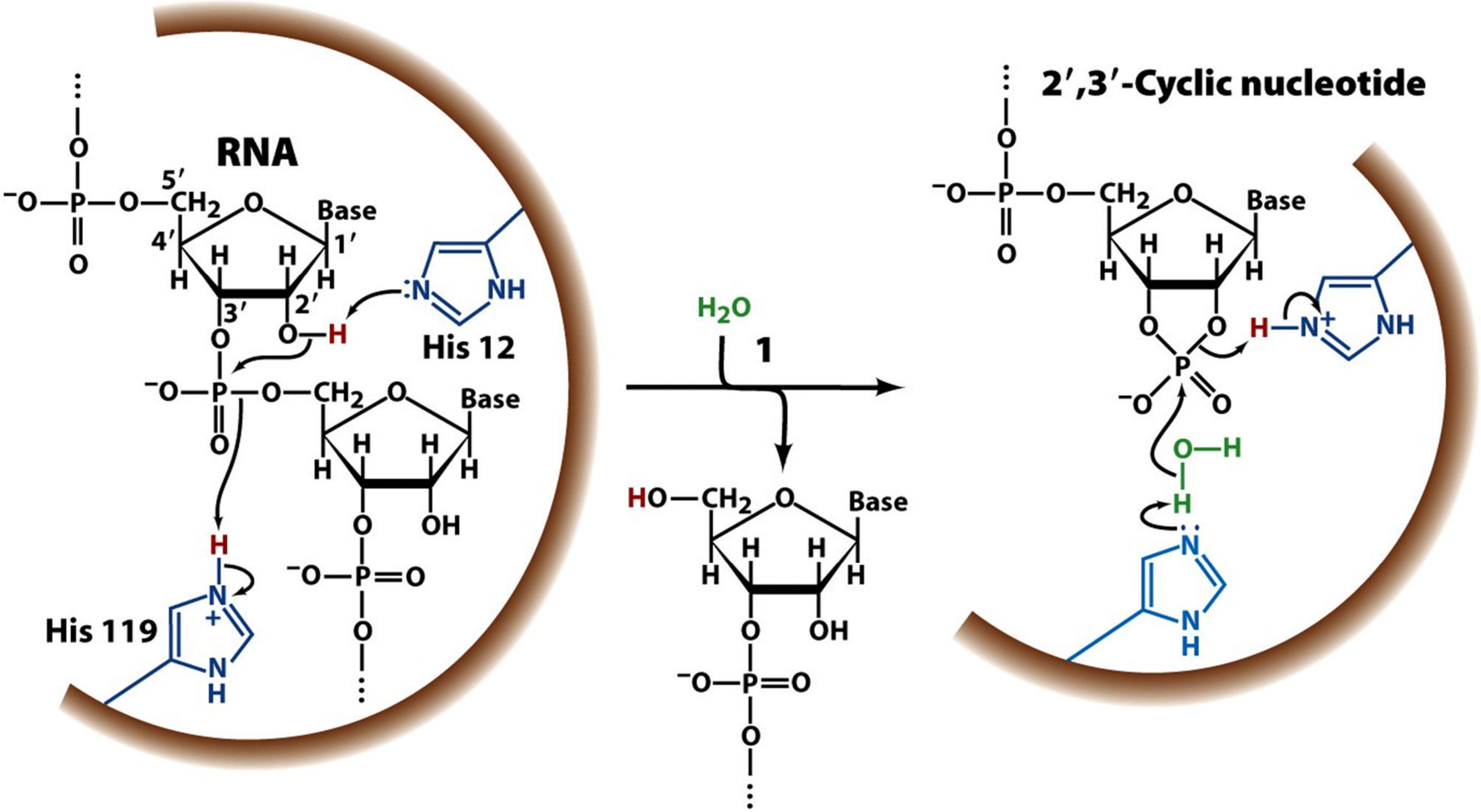
- Metal-ion catalysis: the enzyme uses a metal ion to aid catalysis

Self test: Identify the enzyme class and catalytic mechanisms used.



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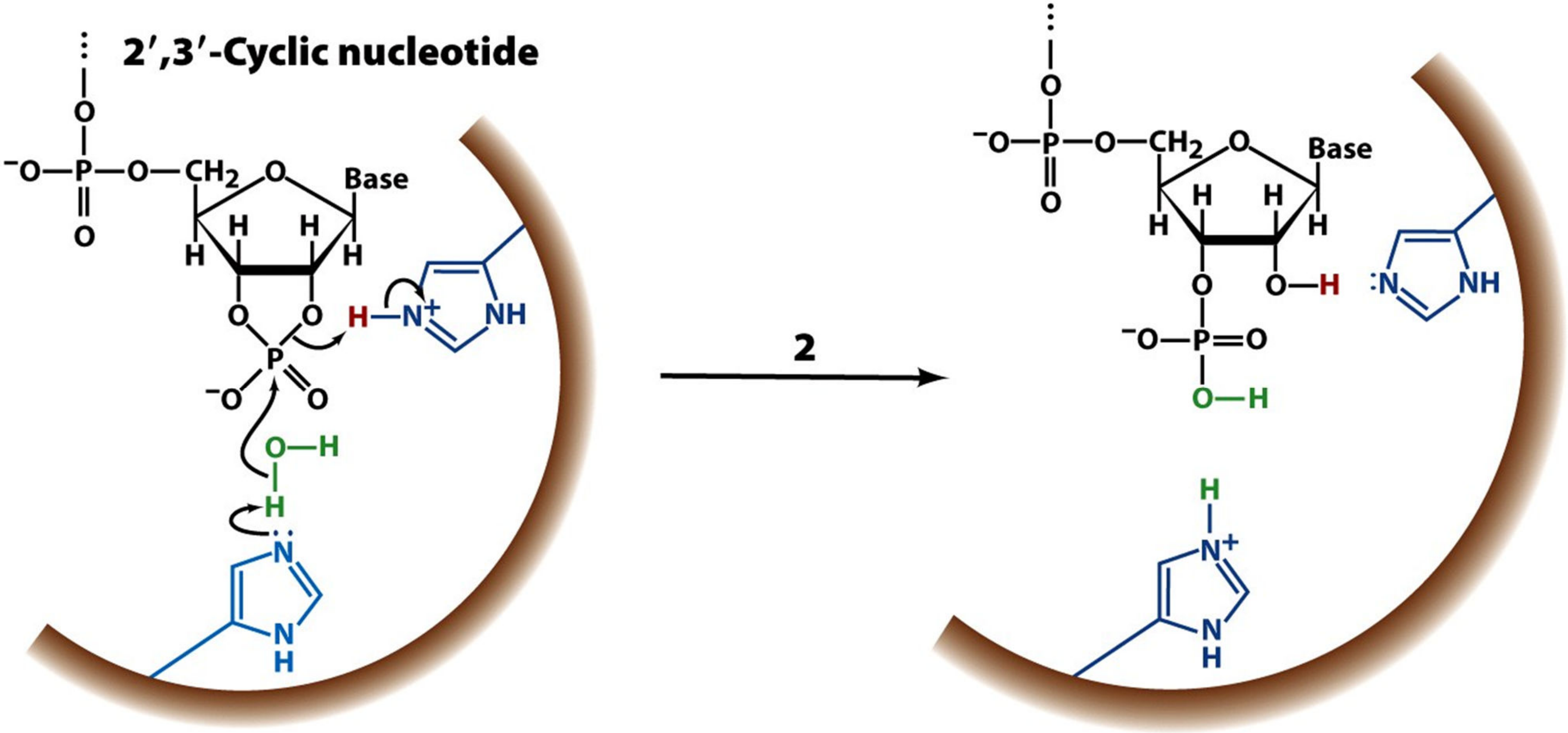
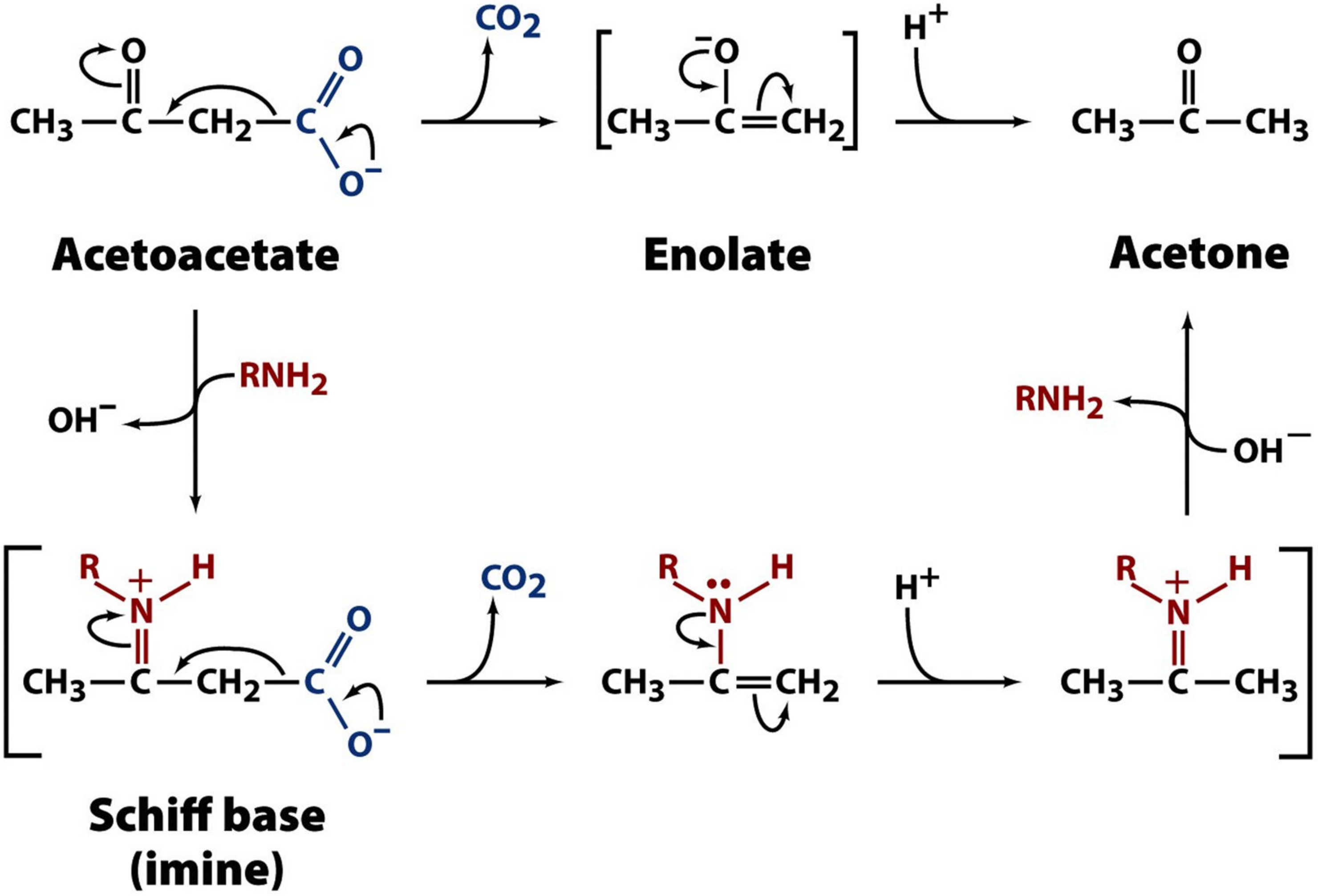
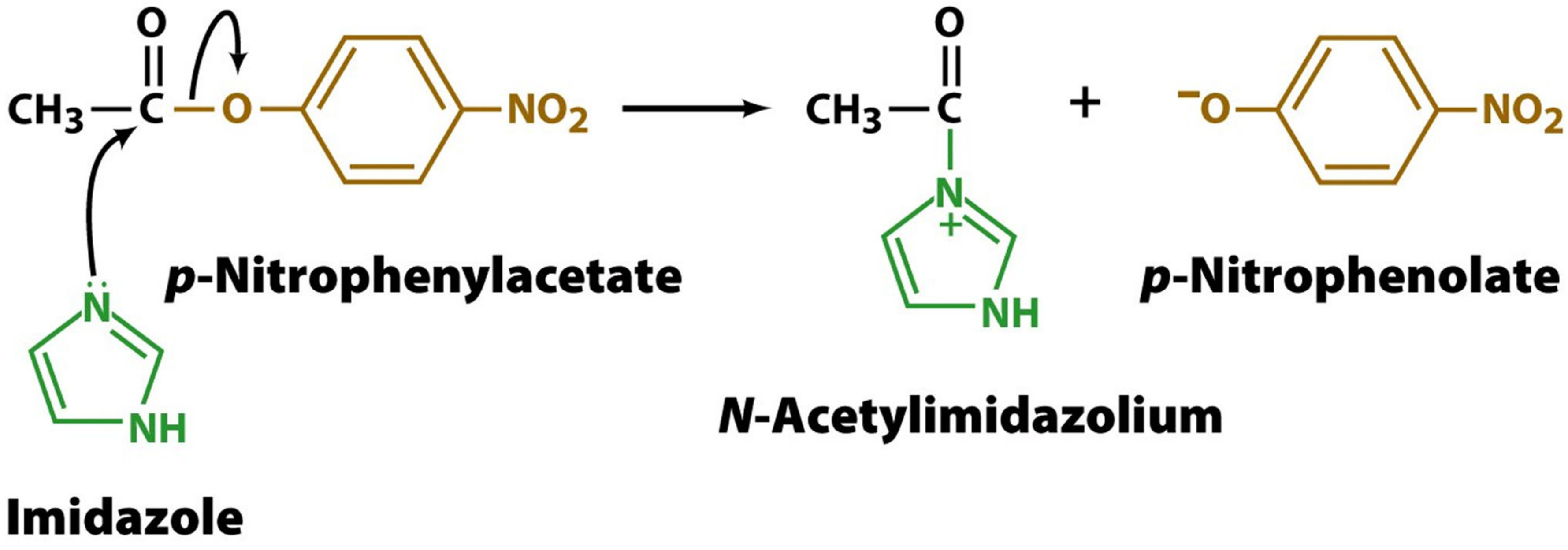


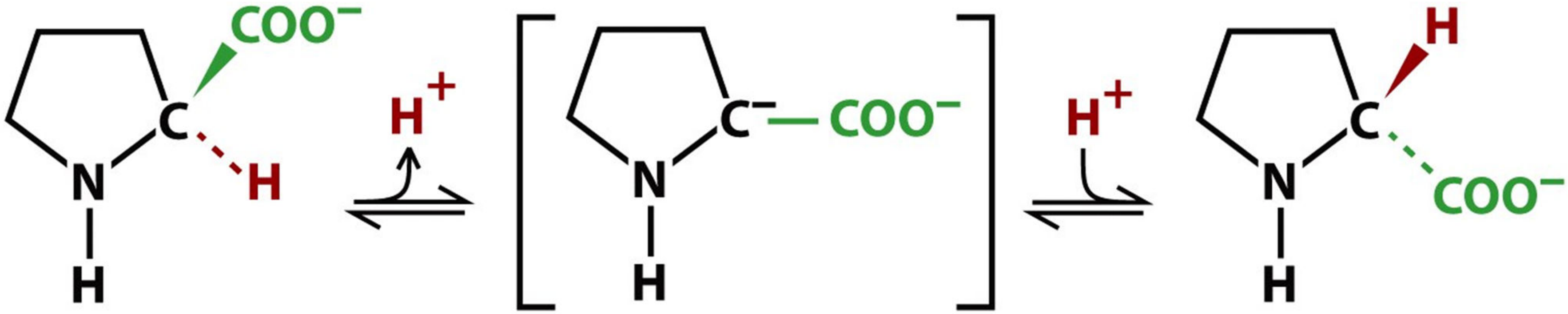
Self test: Identify the enzyme class and catalytic mechanisms used.



Self test: Identify the enzyme class and catalytic mechanisms used.



Self test: Identify the enzyme class and catalytic mechanisms used.



L-Proline

Planar transition state

D-Proline