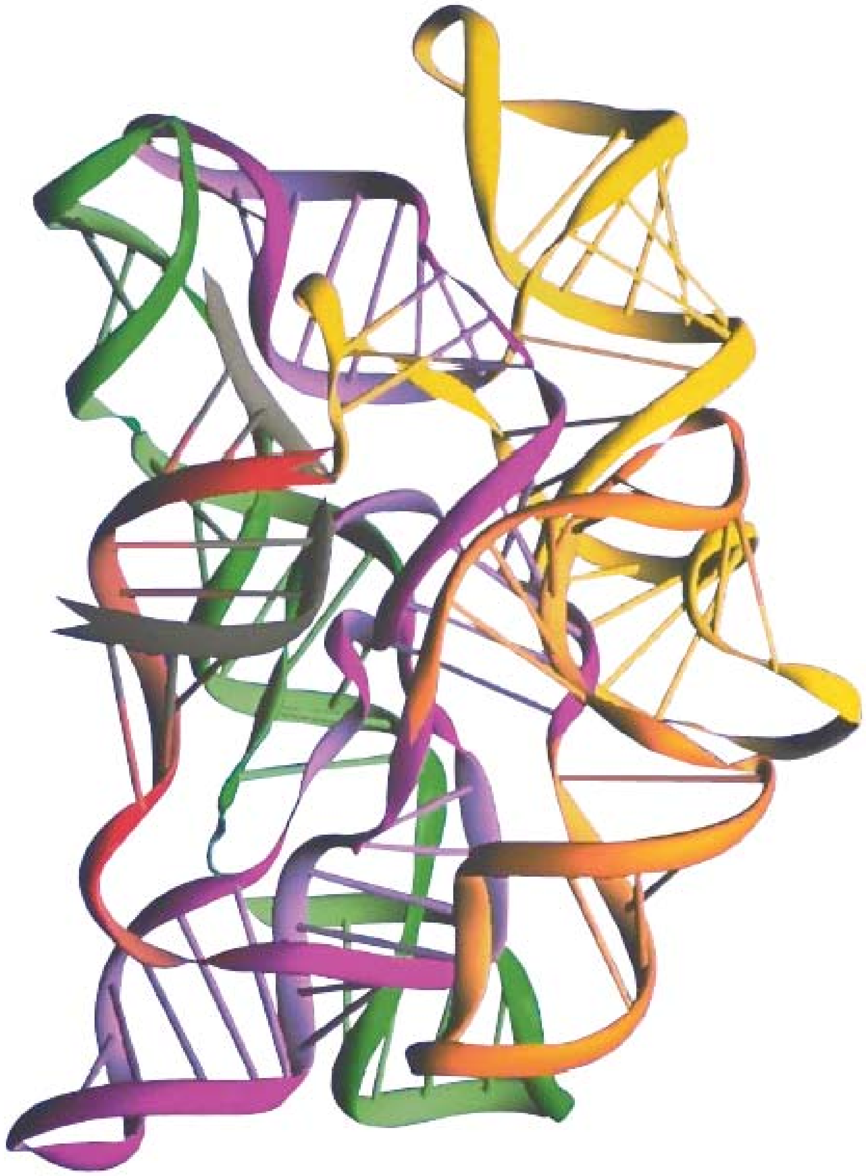
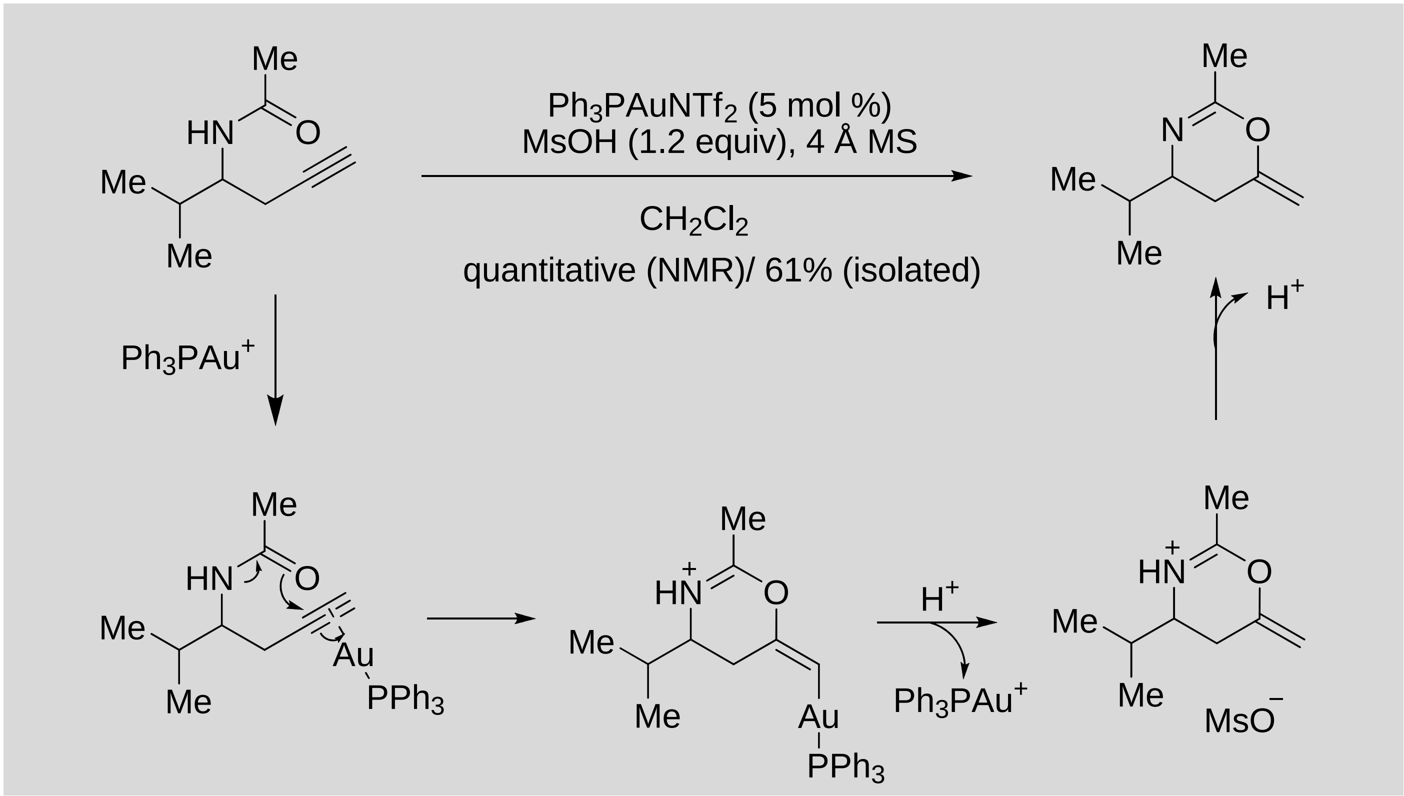
Chapter 23: Catalysis



an RNA catalyst

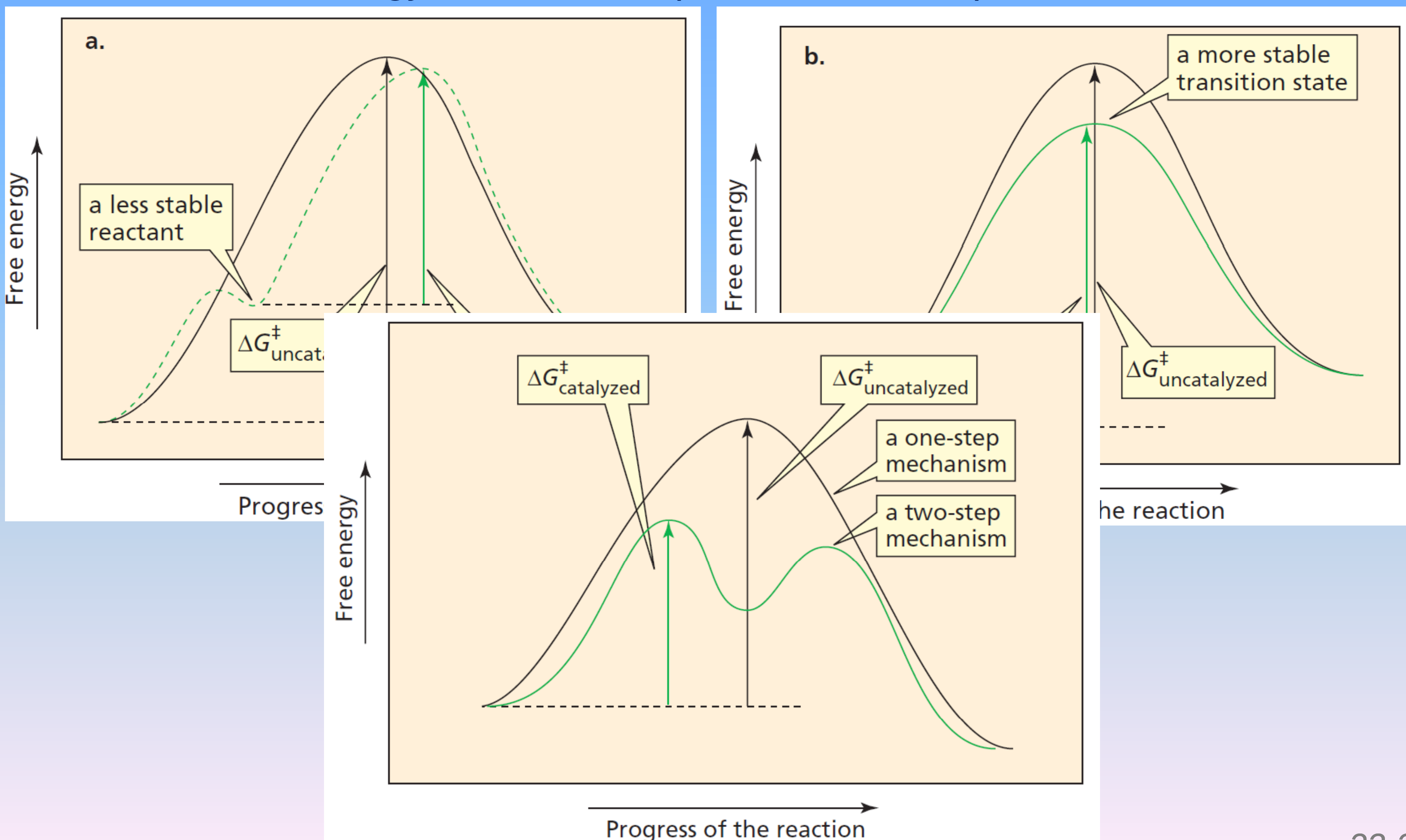
Catalyst and Catalysis: Introduction

- Catalyst is a compound that by its addition to a reaction ***increases the rate of the reaction without itself being consumed or changed at the end of the reaction*** (cycle).
- The reaction is then called being catalyzed.
- The phenomenon of catalyst in accelerating reaction is called catalysis.



Catalyst and Catalysis: Introduction

- Catalyst increases the reaction rate by providing a pathway with lower free energy of activation (reaction kinetics)

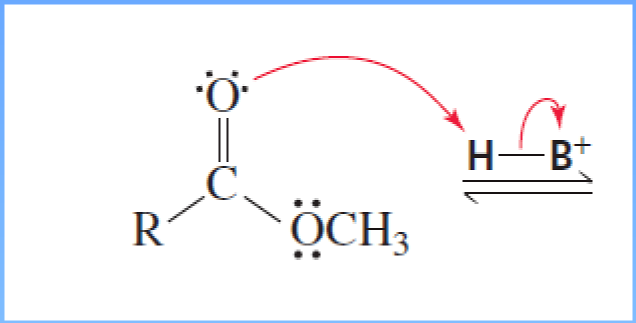


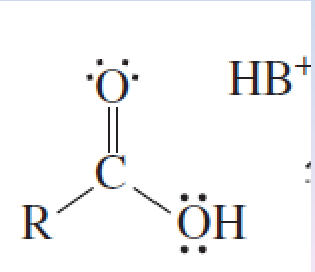
Catalysis in Organic Reactions

- In organic reactions, several ways to accelerate reactions by catalysts:
  - Increase electrophilicity
  - Increase nucleophilicity
  - Increase leaving ability as a nucleofuge (decrease electrophilicity)
  - Increase the stability of a transition state

- Four types of catalysis:
  - acid catalysis
  - base catalysis
  - nucleophilic catalysis
  - metal-ion catalysis

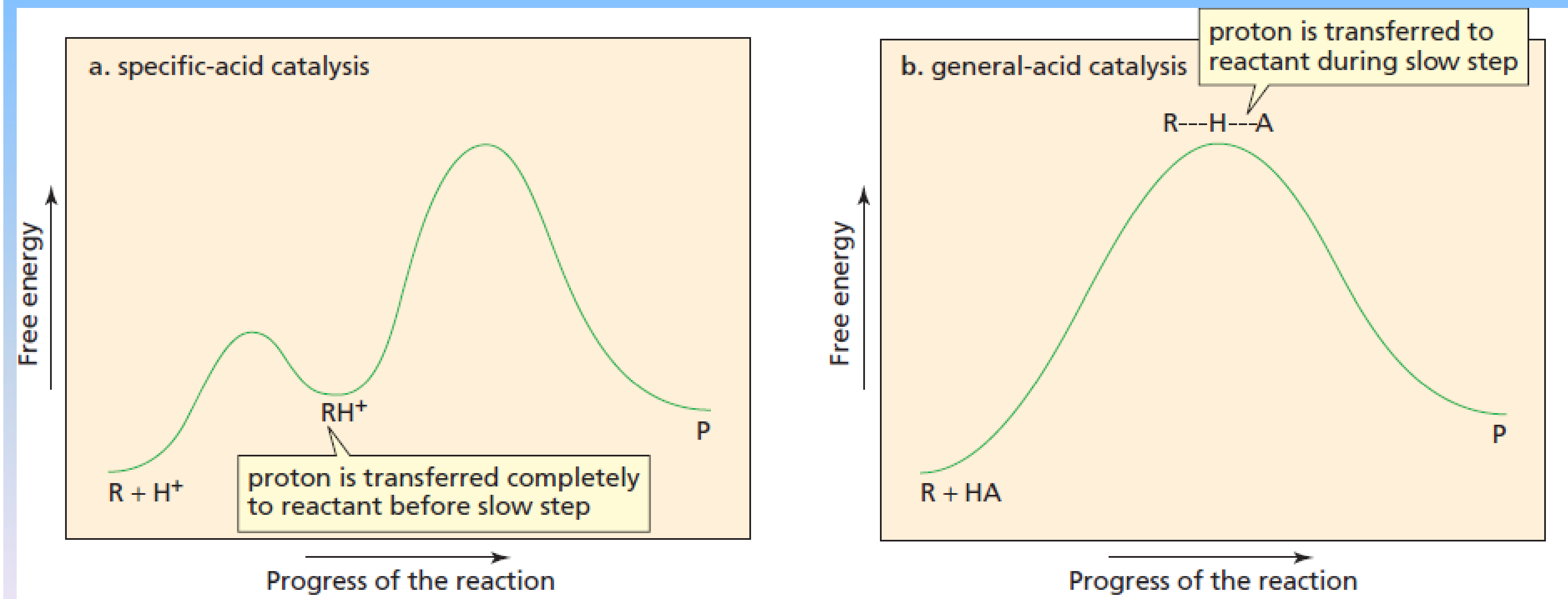
Acid Catalysis: Ester Hydrolysis





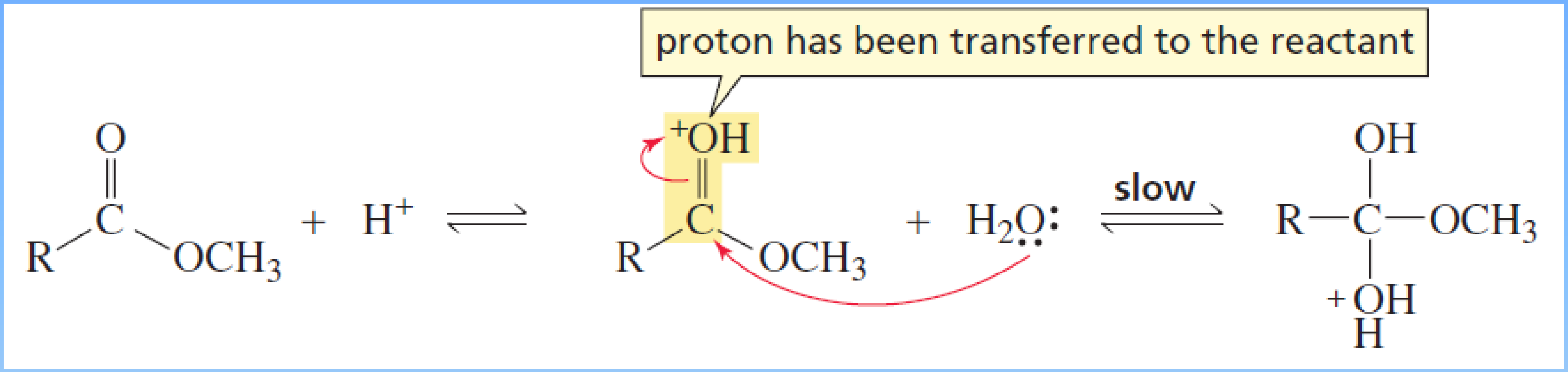
Acid Catalysis

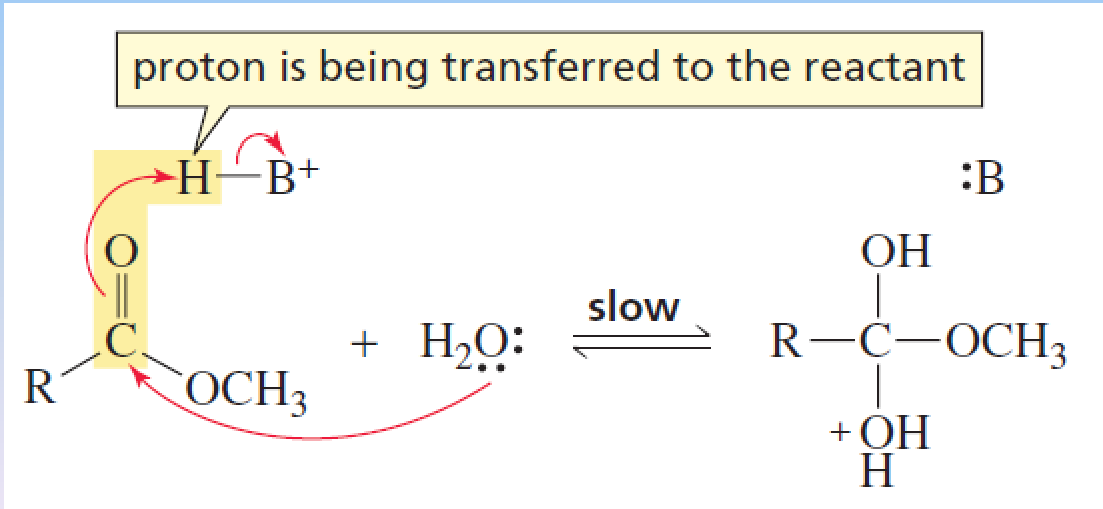
- Specific-acid catalysis and general acid catalysis
  - Specific-acid catalysis: proton is fully transferred before the slow step of the reaction (typically strong acidic conditions, two-stages)
  - General acid catalysis: proton transfer to the reactant during the slow step of the reaction (typically under weak acidic conditions, one stage)



Acid Catalysis

- General-acid catalysis vs. specific-acid catalysis

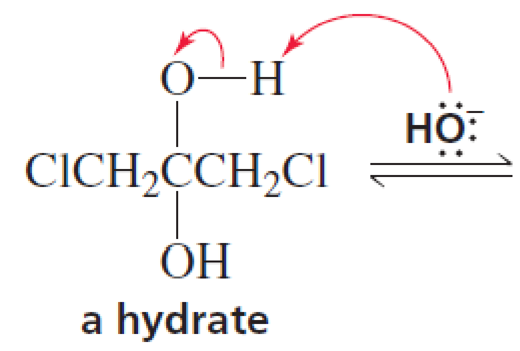




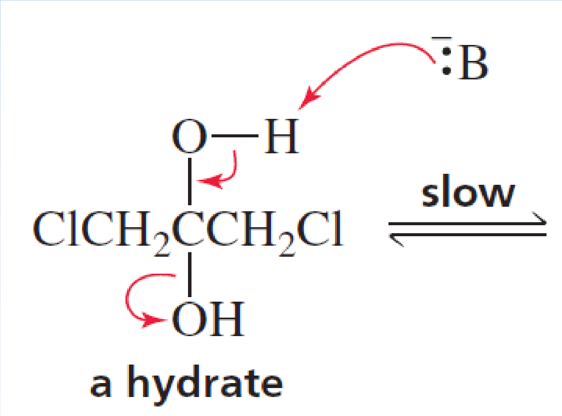
Base Catalysis

- General-base catalysis vs. specific-base catalysis

specific-base-catalyzed dehydration



general-base-catalyzed dehydration



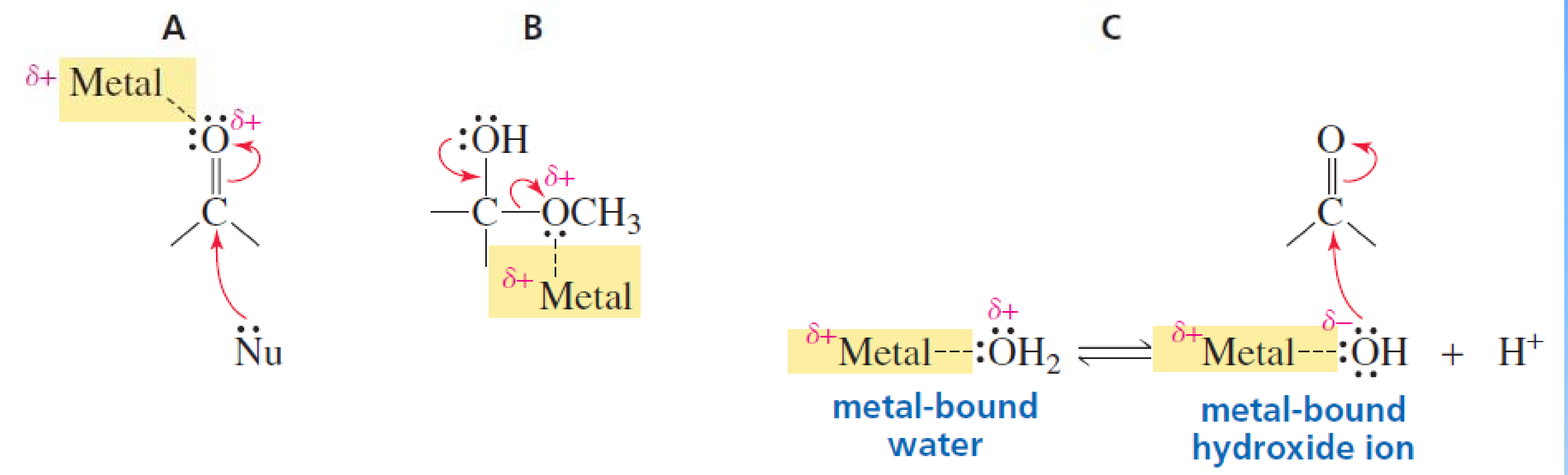
Nucleophilic Catalysis

- The catalyst is nucleophile and forms a covalent bond with reactants/intermediates
- Also called covalent catalysis

$$CH_3CH_2Cl + HO^- \xrightarrow[H_2O]{I^-} CH_3CH_2OH + Cl^-$$

Metal-Ion Catalysis

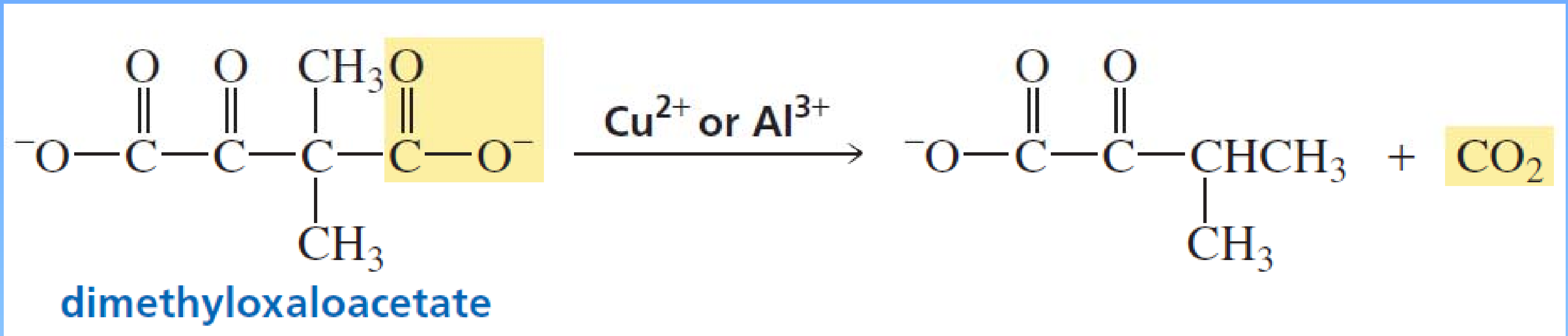
- Lewis acid catalysis (metal ions are Lewis acids)



M^{2+}	pK_a	M^{2+}	pK_a
Ca^{2+}	12.7	Co^{2+}	8.9
Mg^{2+}	11.8	Zn^{2+}	8.7
Cd^{2+}	11.6	Fe^{2+}	7.2
Mn^{2+}	10.6	Cu^{2+}	6.8
Ni^{2+}	9.4	Be^{2+}	5.7

Metal-Ion Catalysis

- Examples:



Metal-Ion Catalysis

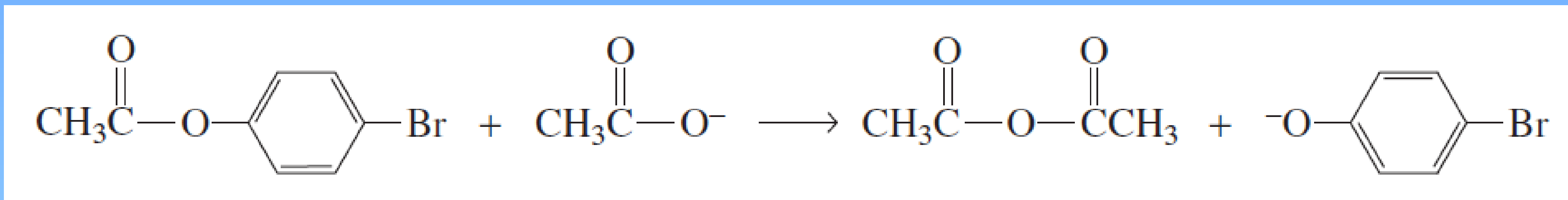
PROBLEM 8

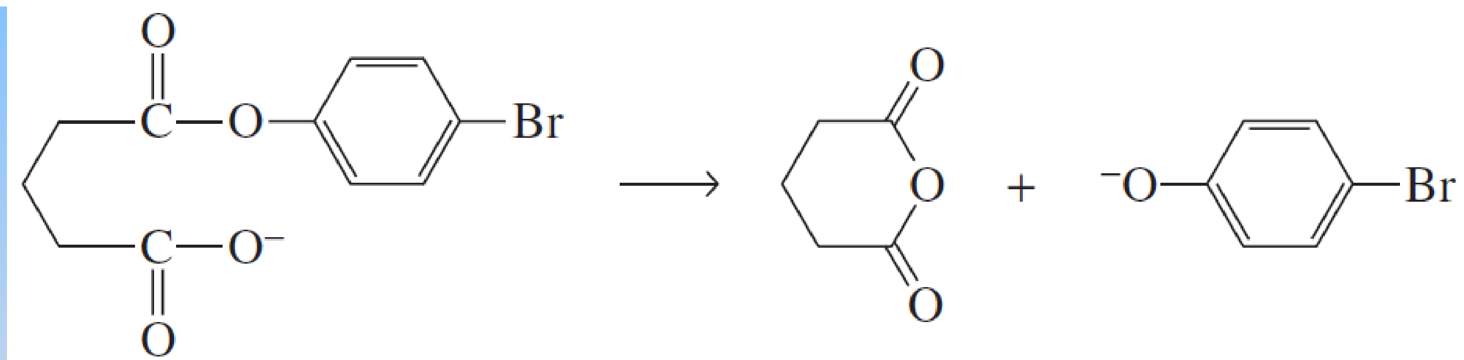
The hydrolysis of glycinamide is catalyzed by Co^{2+}. Propose a mechanism for this reaction.

$$H_2NCH_2\overset{O}{\overset{\|}{C}}NH_2 + H_2O \xrightarrow{Co^{2+}} H_2NCH_2\overset{O}{\overset{\|}{C}}O^- + {}^{+}NH_4$$

Intramolecular Reactions

$$\text{Reaction Rate} = \frac{\text{number of collisions}}{\text{unit of time}} \times \begin{array}{c}\text{fraction with}\\ \text{sufficient energy}\end{array} \times \begin{array}{c}\text{fraction with}\\ \text{proper orientation}\end{array}$$





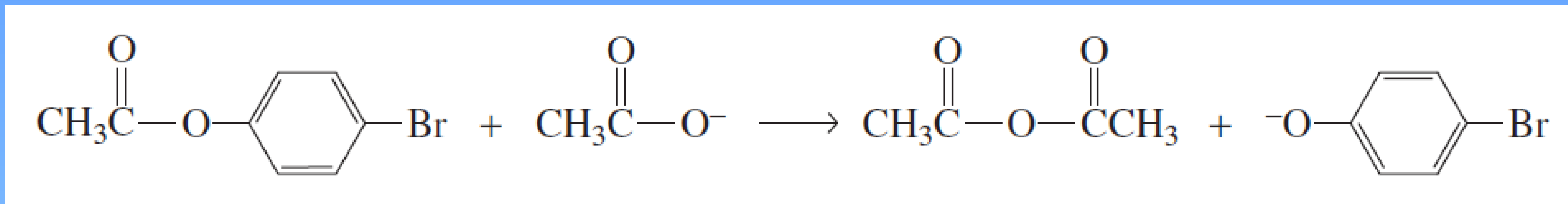
1000 times faster

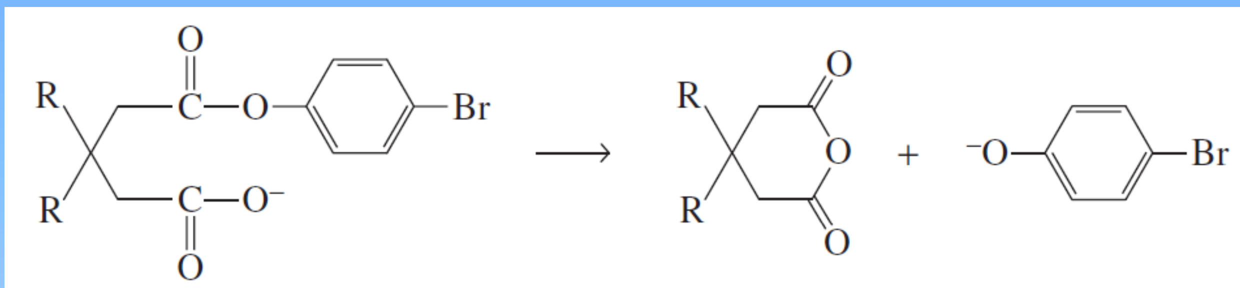
$$\text{relative Rate} = \frac{\text{first order rate constant}}{\text{second order rate constant}} = \frac{\text{time}^{-1}}{\text{time}^{-1}\ \text{M}^{-1}} = \text{M}$$

effective molarity

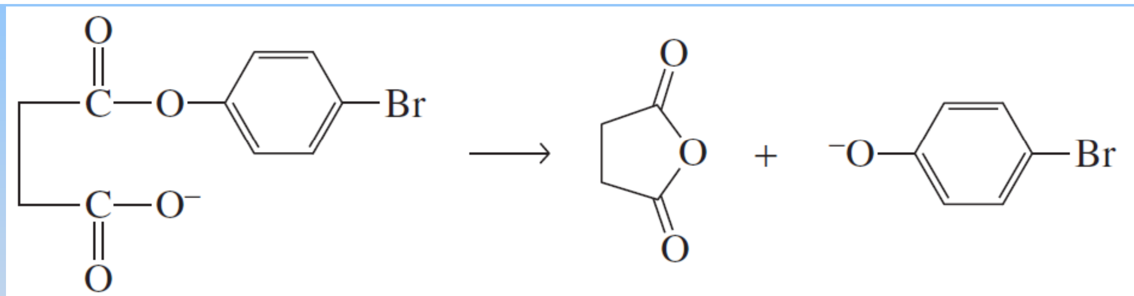
- ***Effective molarity (EM) is the concentration of the reactant that would be required in an intermolecular reaction for it to achieve the same rate as intramolecular reaction***

Intramolecular Reactions

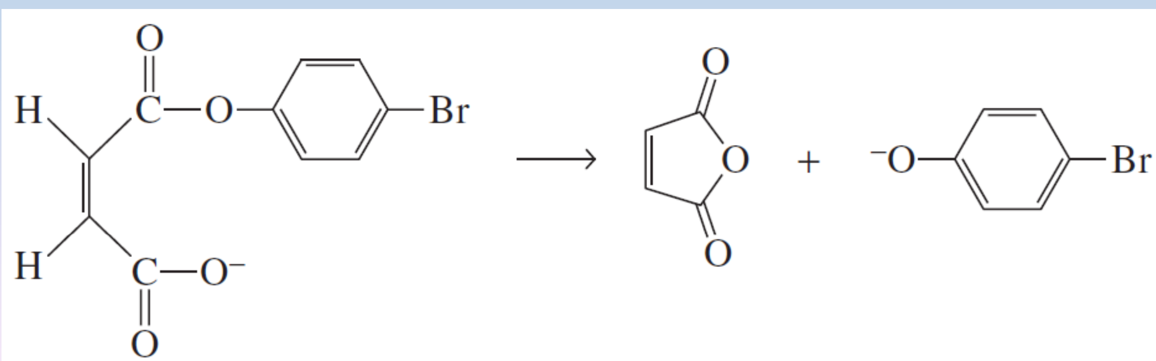




R = Me, EM = 2.3 x 10^4 M
R = iPr, EM = 1.3 x 10^6 M



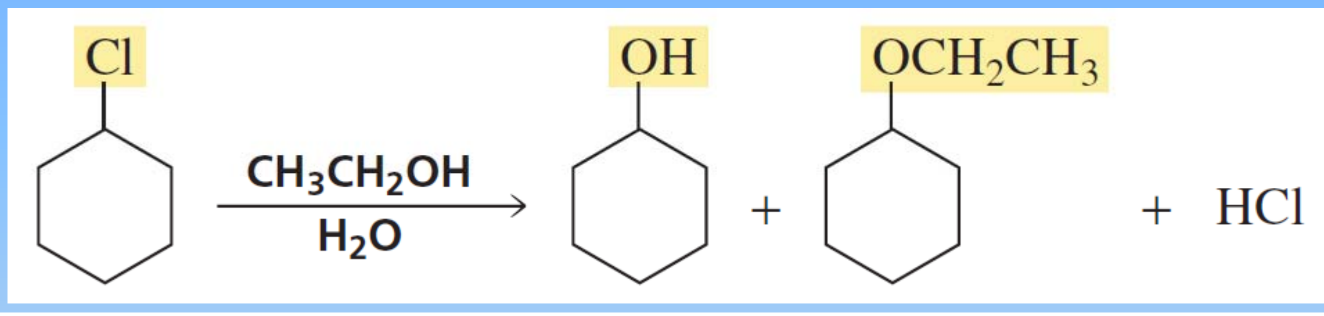
EM = 2.2 x 10^5 M

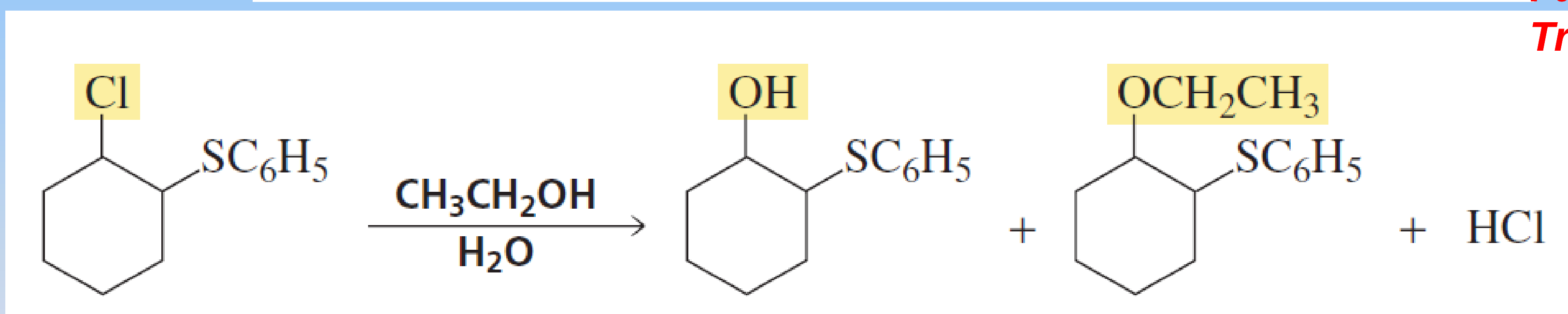


EM = 1 x 10^7 M

Intramolecular Catalysis

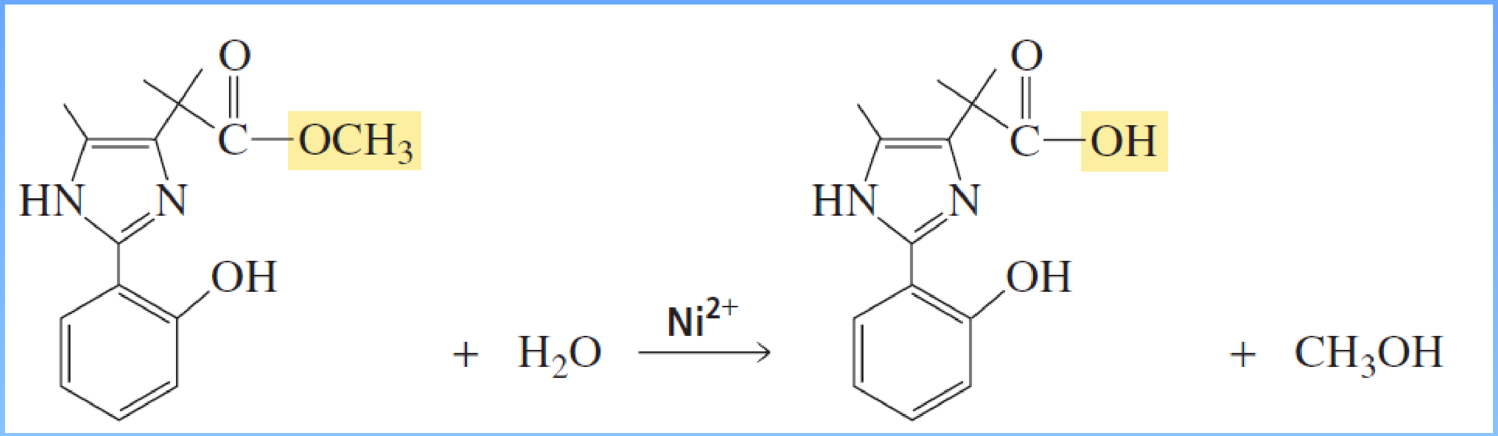
- A catalyst is embedded or covalently bonded to substrates
- Also called anchimeric effect/assistance
- Due to intramolecularity, the catalysis should be more efficient.



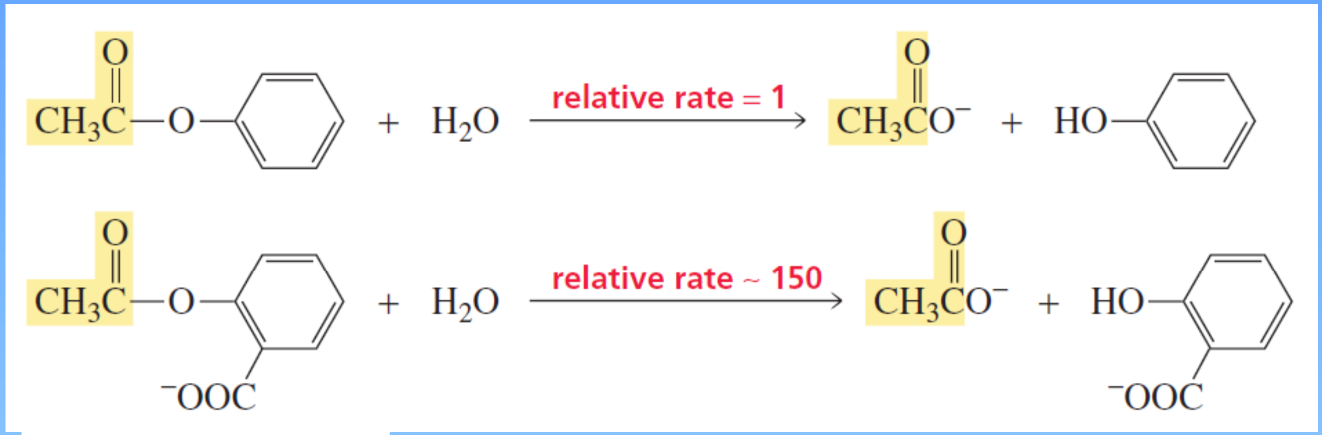


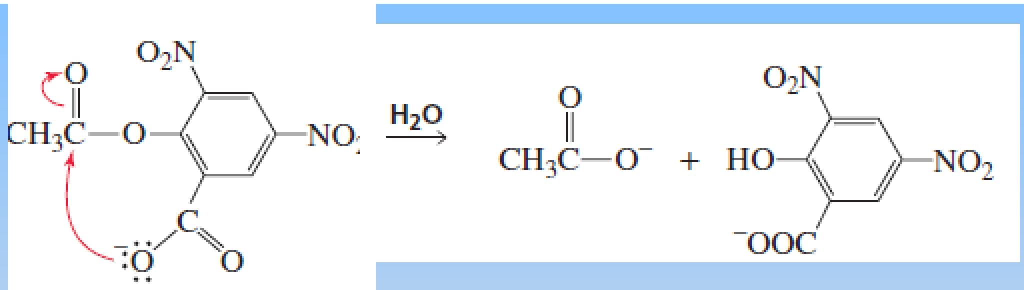
70000 times Faster in the Trans isomer

Intramolecular Catalysis: Example



Intramolecular Catalysis: Example

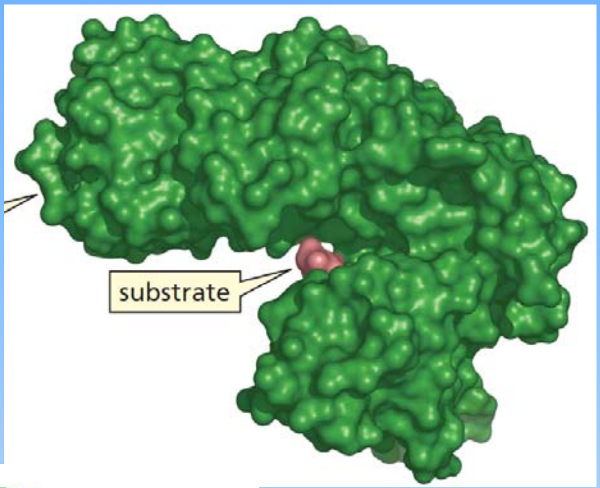




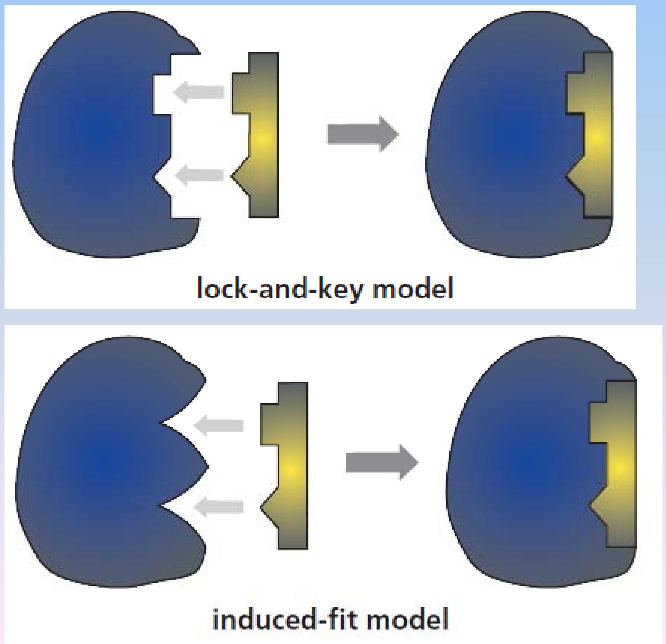
an ester

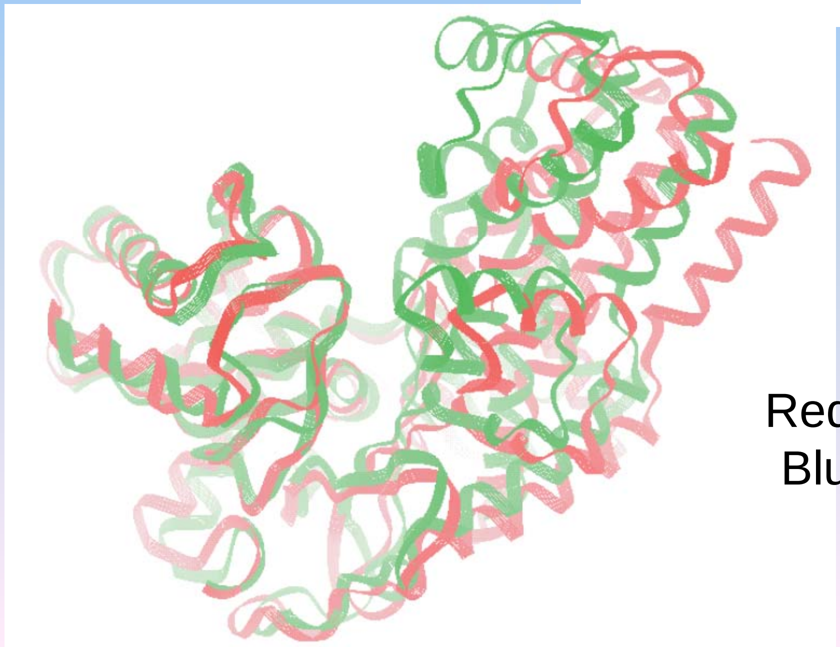
Catalysis in Biological Reactions

- Most biological catalysts are enzymes (belongs to globular proteins)
- Substrates and active sites (where the reaction occurs)



- Substrates bound to the active site
  - Specificity (molecular recognition)
    - Lock-and-key model
    - Induced-fit model



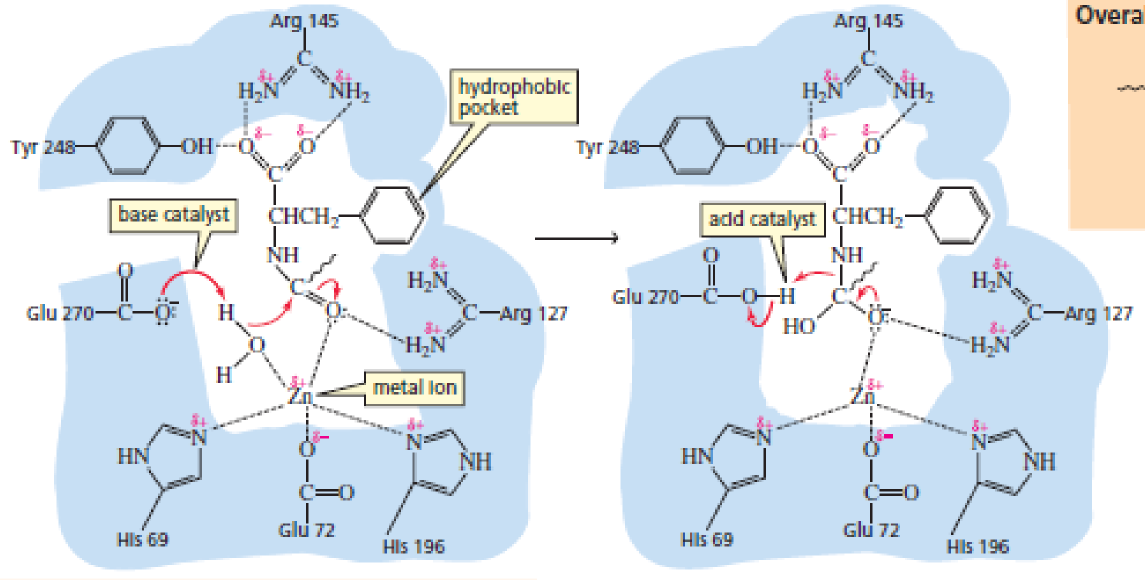


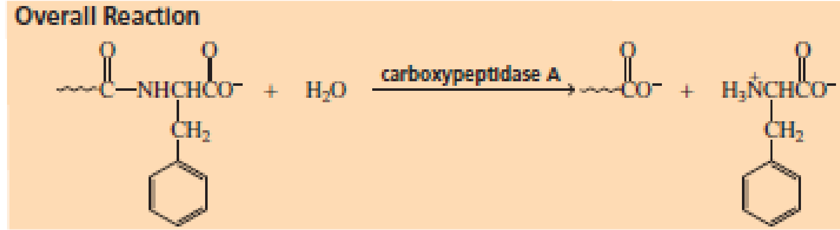
Hexokinase
Red: before binding
Blue: after binding

Enzyme Catalysis

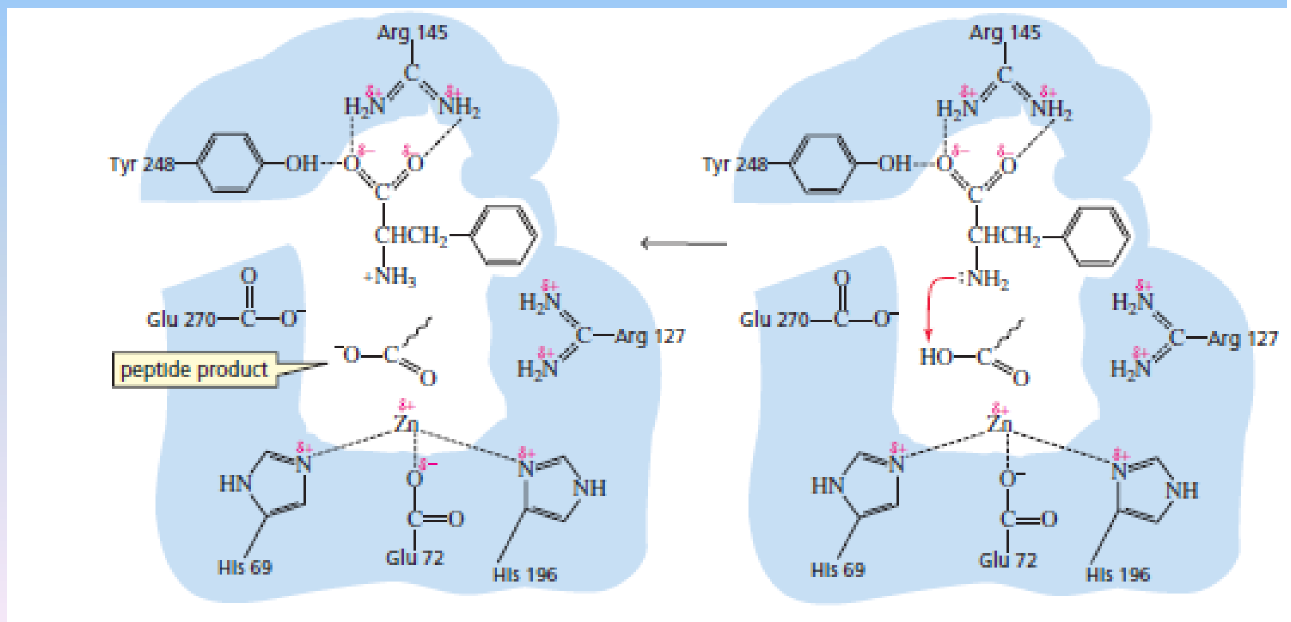
- How do enzymes do catalysis?
  - Reacting groups are brought together in a proper orientation
  - Some of the amino acid side chains as well as bounded metal ions as catalyst
  - Stabilizing the transition states and intermediates via van der Waals interactions, electrostatic interactions, and H-bonding.
- Naming of enzymes
  - End typically with ‘ase’, indicating breaking the bond
    - Peptidase: breaking the peptide bond
    - Esterase: breaking the ester bond
  - Synthase
    - Synthesizing instead of breaking it down.

Carboxypeptidase A



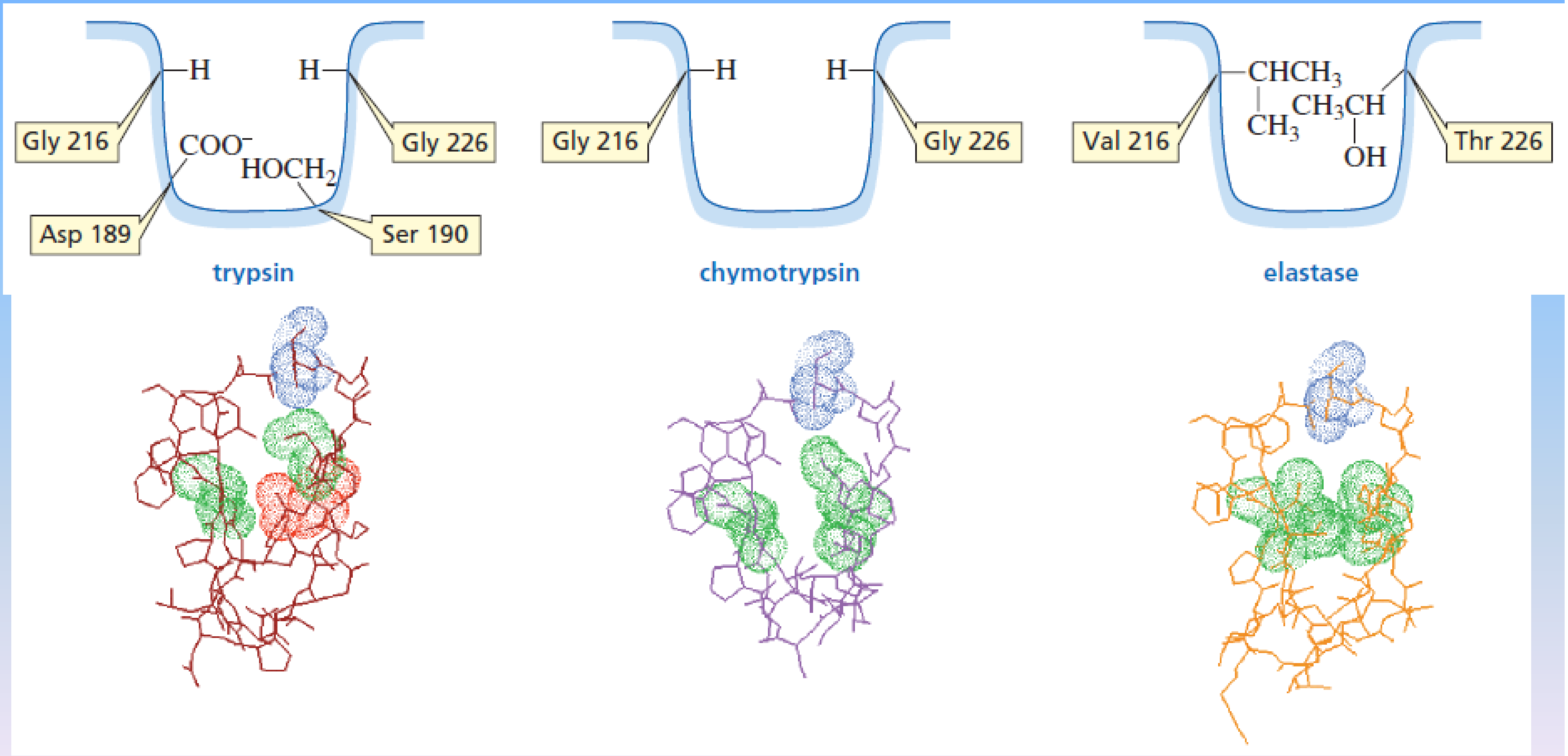


- Metalloenzyme (enzymes containing tightly bound metal ions)
- Hydrolyze C-terminal except lysine and arginine.

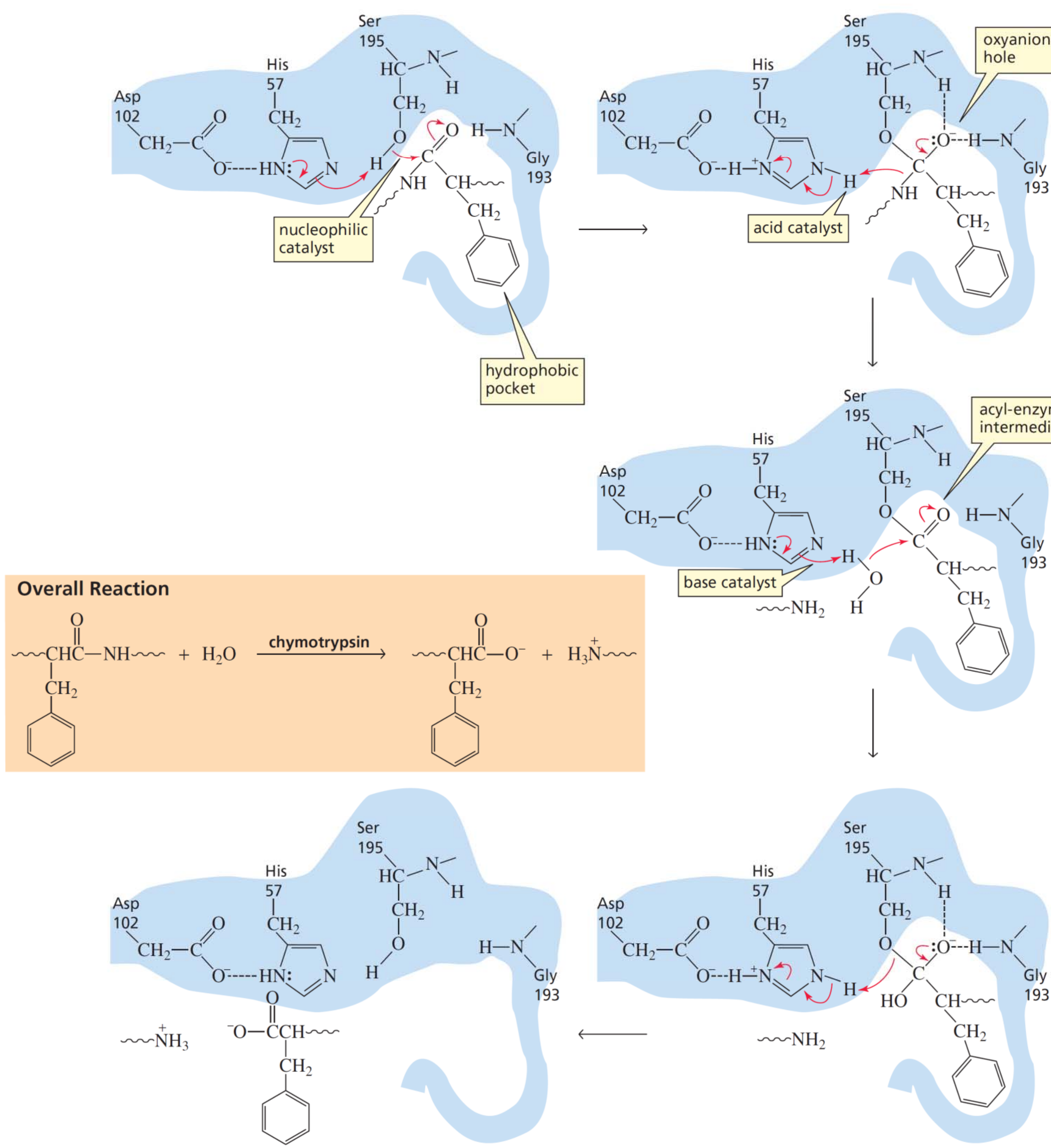


Serine Proteases

- Trypsin, chymotrypsin and elastase are members of endopeptidases known as serine proteases

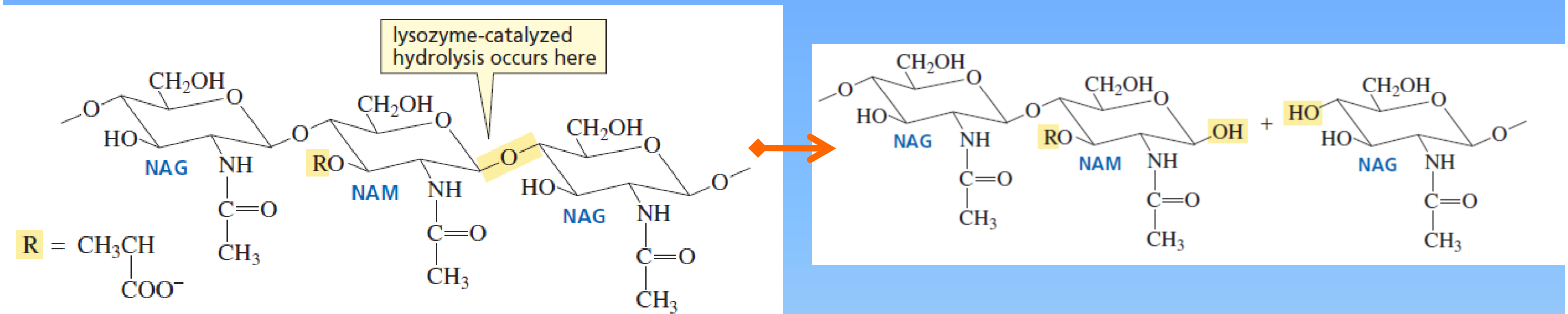


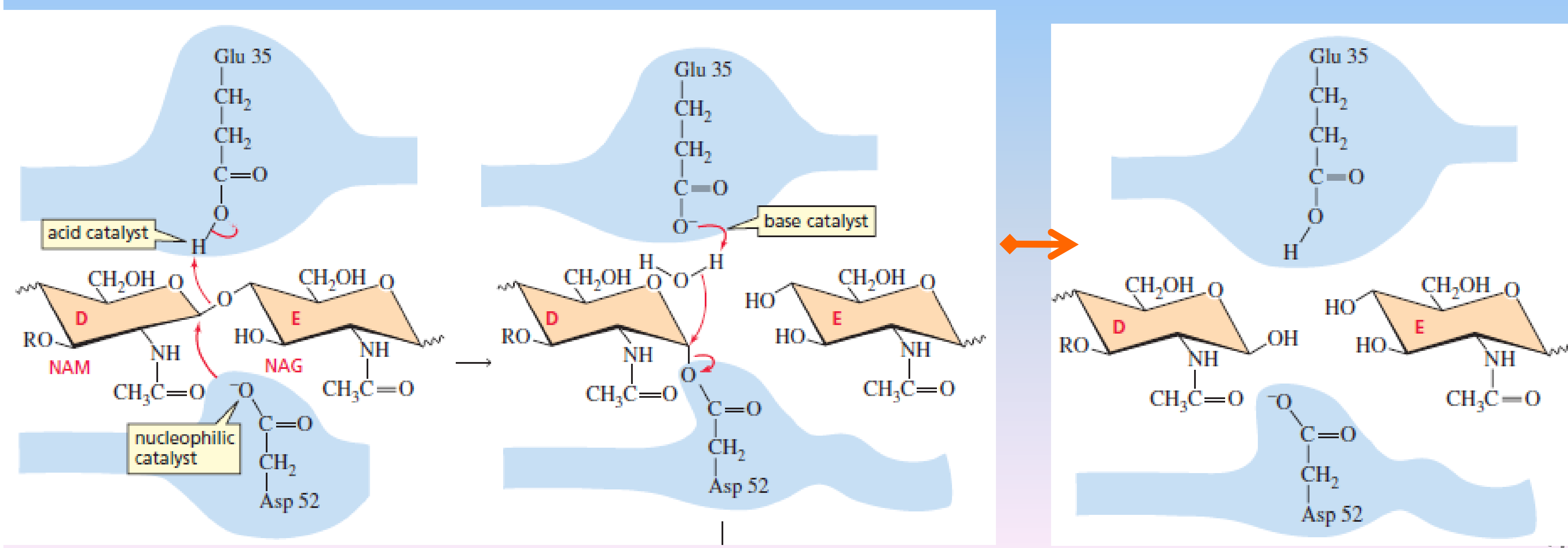
- Proposed mechanism for chymotrypsin-catalyzed hydrolysis



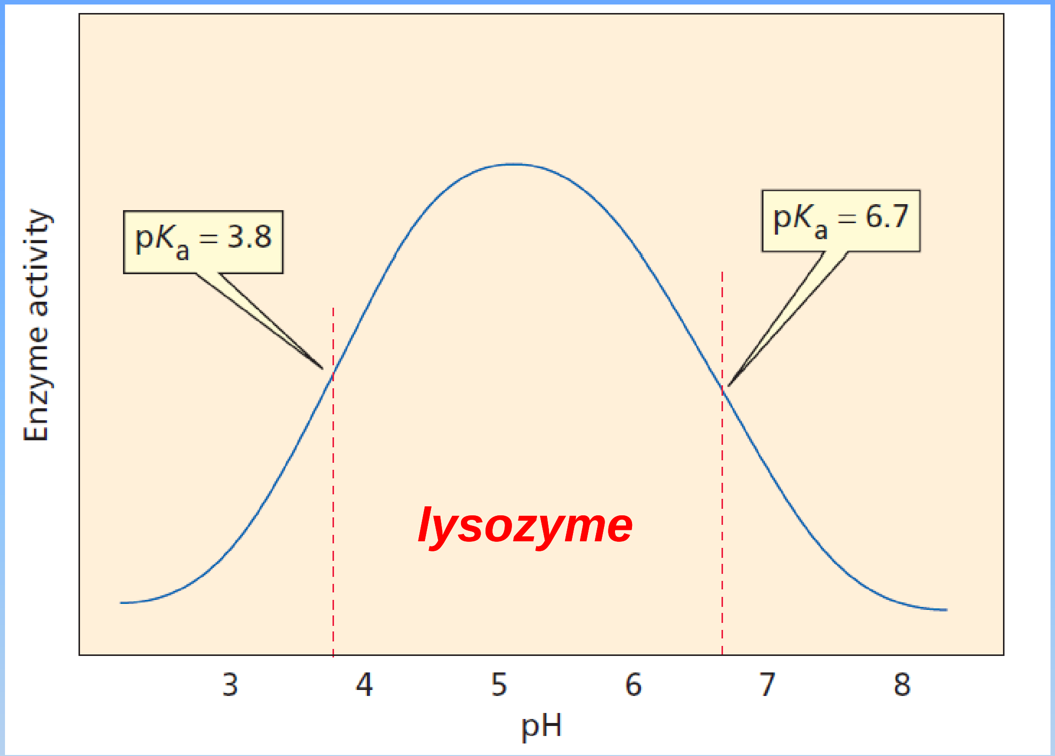
Lysozyme

- Catalyze the hydrolysis of the bacterial cell wall NAM-NAG bond (NAM: *N*-Acetylmuramic acid)



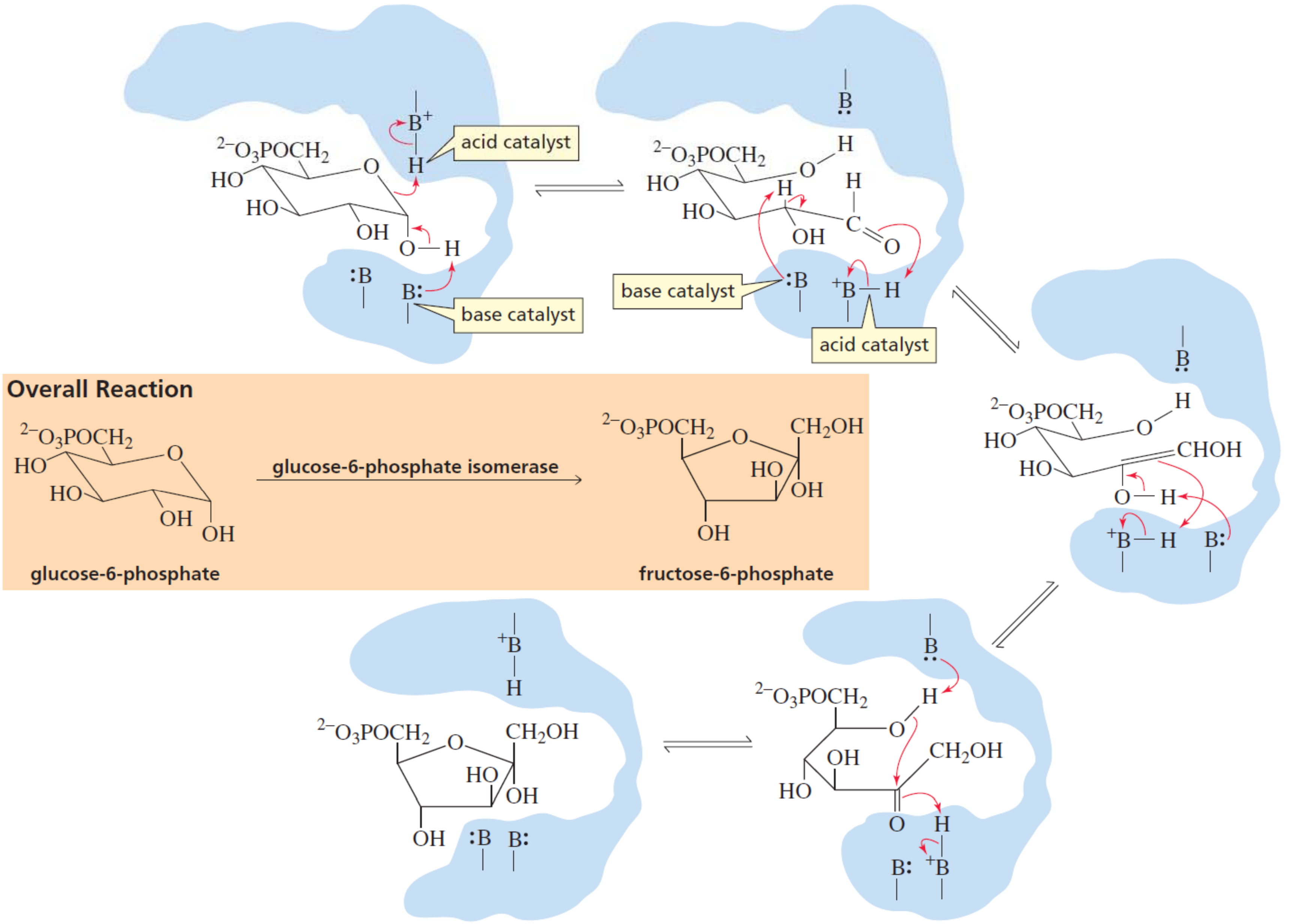


Protein pH-Rate Profile

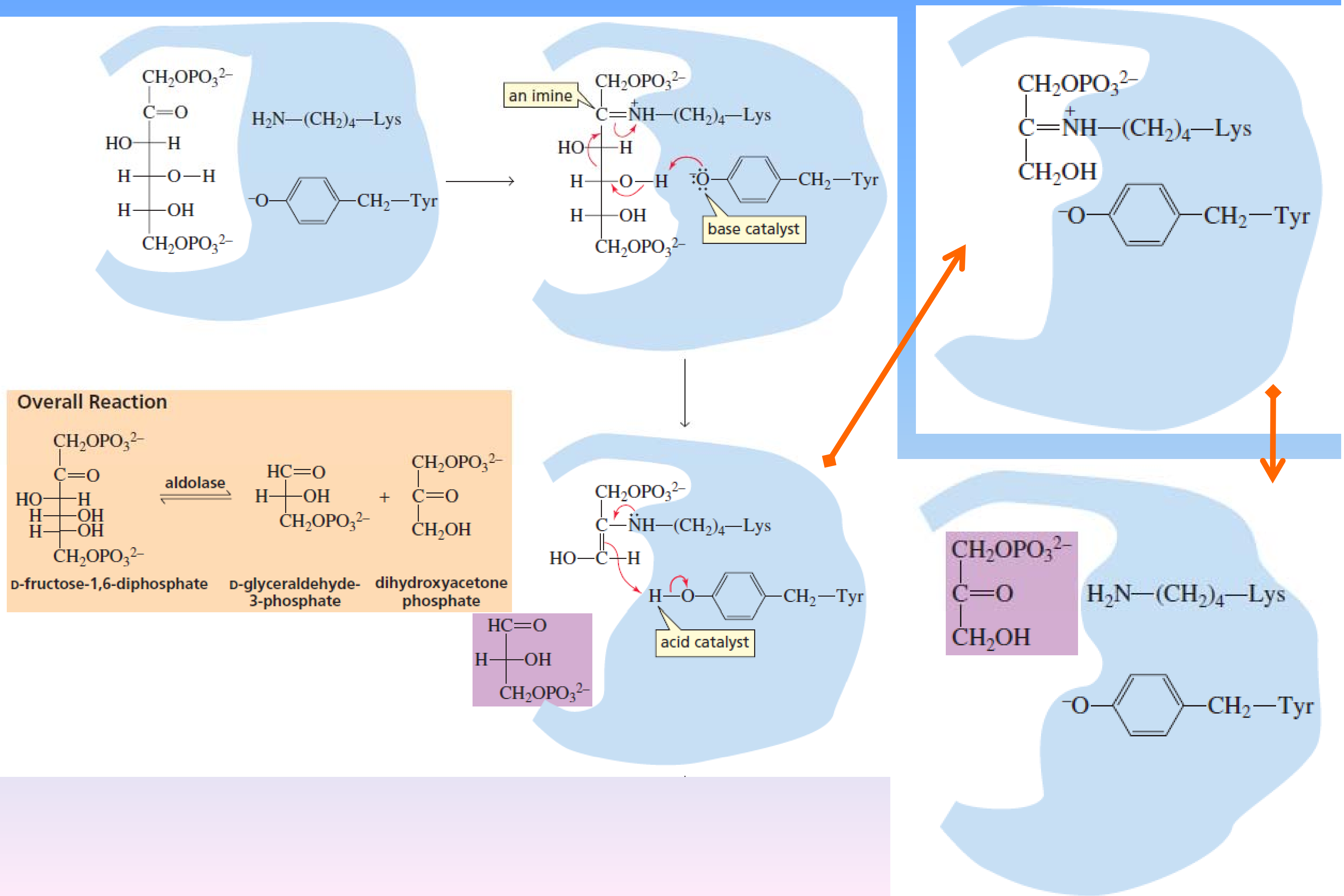


- The pHs at which the enzyme are 50% active corresponds to the pKa of enzyme's catalytic groups (as long as those values are at lease 2 units apart.
- Why pKa of Asp52 is 3.8 but pKa of Glu35 is 6.7 instead of 4.25 in its free form?

Glucose-6-Phosphate Isomerase



Aldolase


Overall Reaction
aldolase
D-fructose-1,6-diphosphate
D-glyceraldehyde-3-phosphate
dihydroxyacetone phosphate
an imine
base catalyst
acid catalyst
H2N—(CH2)4—Lys
CH2—Tyr