CONCEPT: COVALENT CATALYSIS

4) Covalent Catalysis

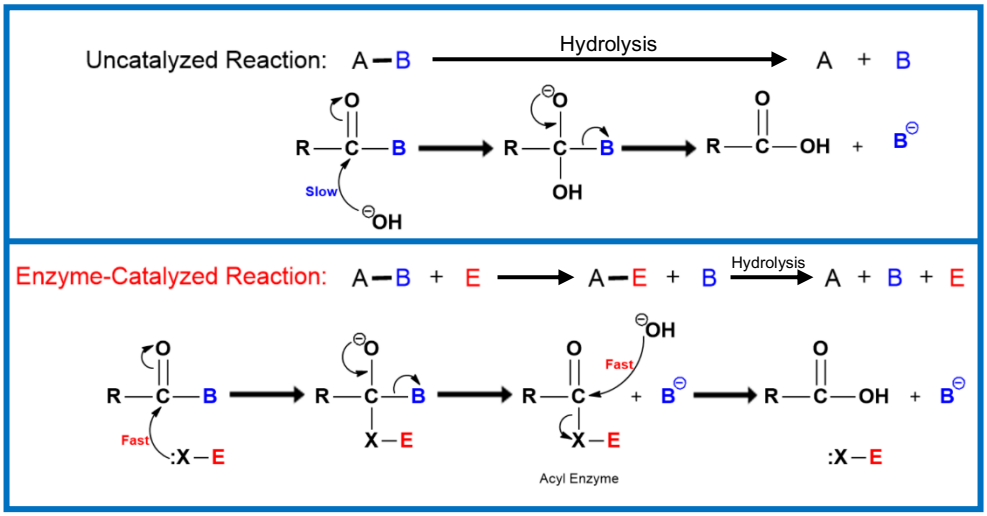
●*Covalent Catalysis*: transient/temporary _____ bonds formed between the enzyme & substrate as an intermediate.

□ Still _____ overall reaction rate (compared to uncatalyzed rate) despite a longer pathway.

●Enzymes have amino acids that can act as _____ (donates electrons) & attack substrates.

□ Any covalent bonds formed with the enzyme must eventually be _____ to restore the original enzyme.

EXAMPLE: Covalent Catalysis.



PRACTICE: An enzyme has two key catalytic residues, Glu 35 (pK_a= 5.9) and Asp 52 (pK_a= 4.5). Which of the following is likely true about the mechanism for this enzyme if the optimum pH = 5.2?

a) Glu 35 is more likely a nucleophile than Asp 52.
b) Glu 35 is more likely a general acid than Asp 52.
c) Both a and b are true.
d) a, b & c are false.

PRACTICE: Which of the following mechanisms is not used by enzymes for catalysis?

a) General Acid-base catalysis.
b) Induced fit of enzyme to transition state.
c) Destabilizing the transition state.
d) Providing complementary electrostatics.
e) Binding of metal ions.
f) Specific Acid-Base Catalysis.
g) a & c
h) c & f.
i) b, c & f.

CONCEPT: COVALENT CATALYSIS

PRACTICE: Which catalytic mechanism uses an electrophilic cofactor to stabilize a negative charge on an intermediate?

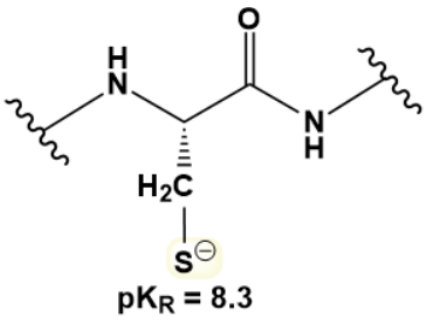
a) Acid-base catalysis.
b) Electrostatic catalysis.
c) Covalent catalysis.
d) Metal ion catalysis.

PRACTICE: Which of the following catalytic mechanisms proceeds via noncovalent interactions?

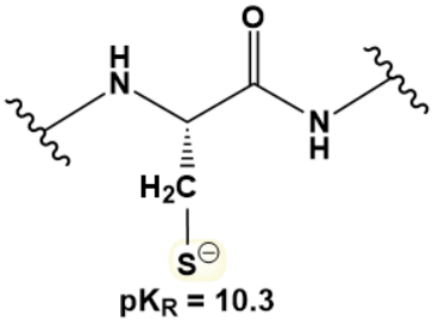
a) Acid-base catalysis.
b) Electrostatic catalysis.
c) Covalent catalysis.
d) Metal ion catalysis.
e) b and d.
f) a, b & d.

PRACTICE: Suppose that the covalent catalytic mechanism of an enzyme depends on a single active site amino acid (Cys), whose $pK_a = 8.3$. A mutation in a nearby amino acid residue of the enzyme only slightly alters the microenvironment so that the pK_a of the Cys residue increases to 10.3. Would this mutation cause the enzyme-catalyzed reaction rate to increase or decrease? Explain.

a) Reaction rate increases.
b) Reaction rate decreases.



$pK_R = 8.3$



$pK_R = 10.3$