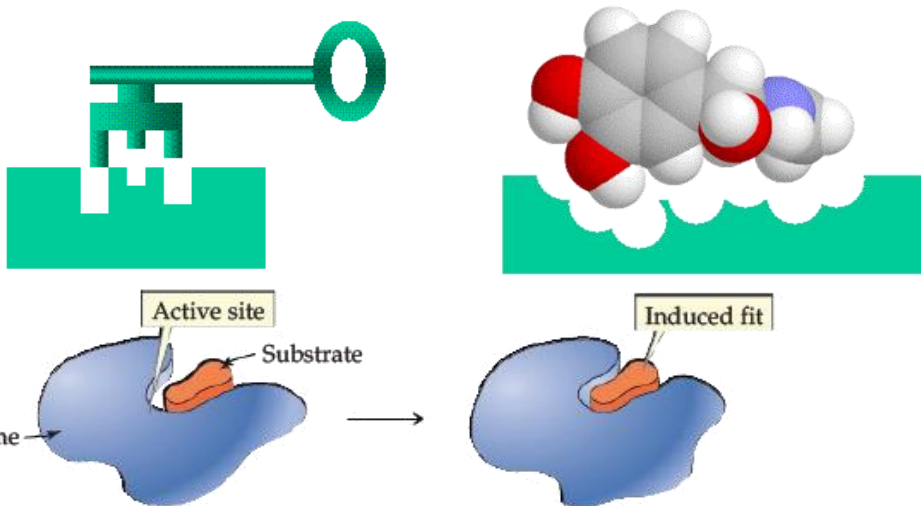
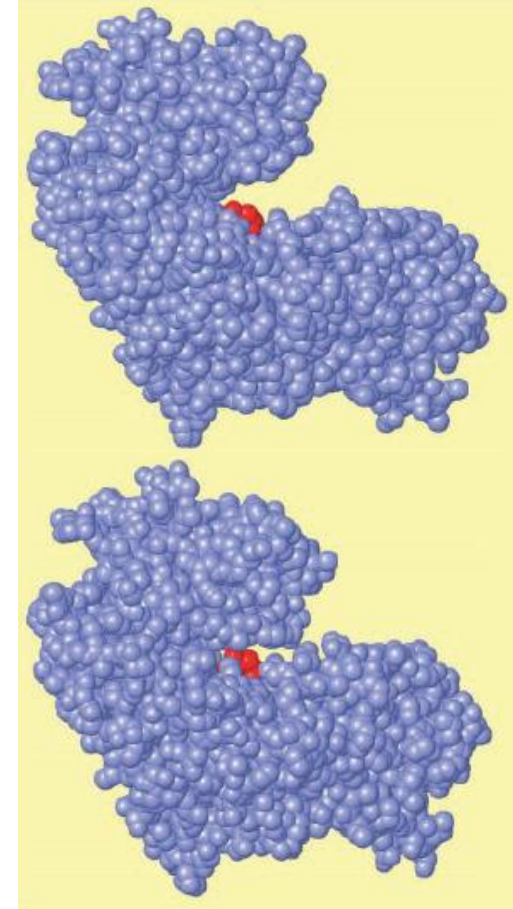
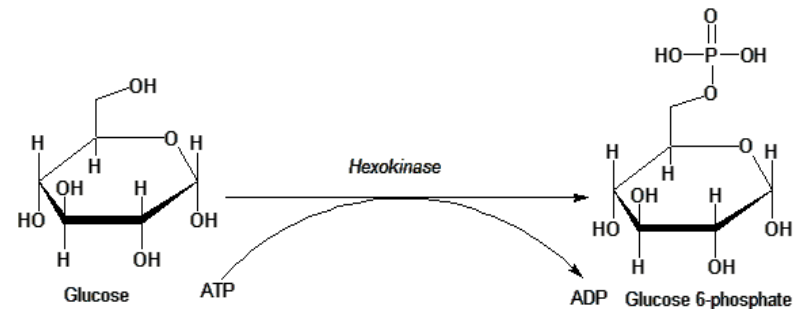


How Do Enzymes Work?

- Binding leads to formation of transition-state
- Usually, substrate binds by non-covalent interactions to the active site
- The catalyzed reaction takes place at the active site, usually in several steps
- Two models, lock-and-key vs. induced-fit model
- Glucose and hexokinase, phosphorylation

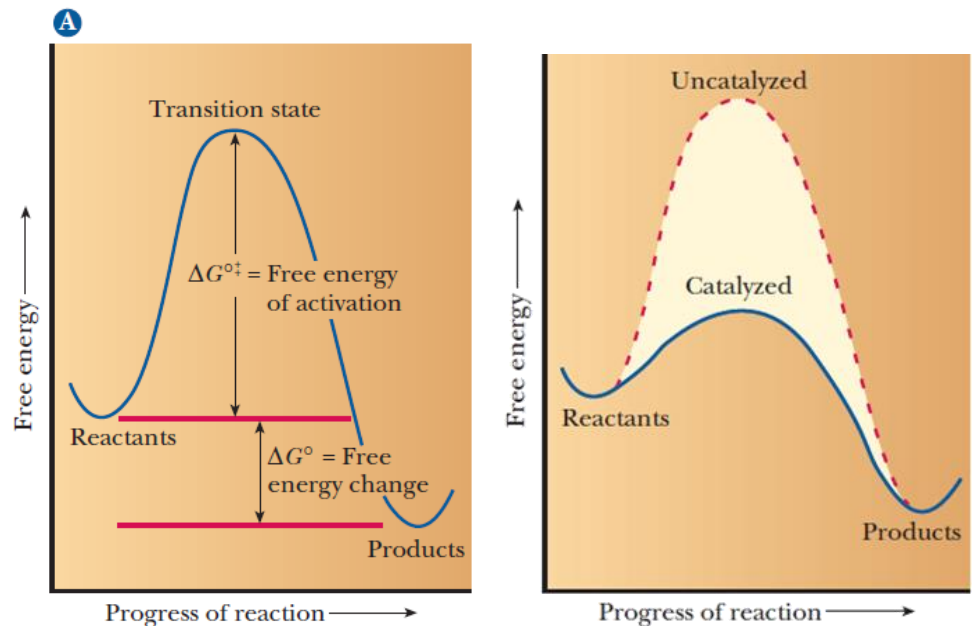


Improving the binding site for ATP & excluding water (might interfere with the reaction)



How do enzymes work?

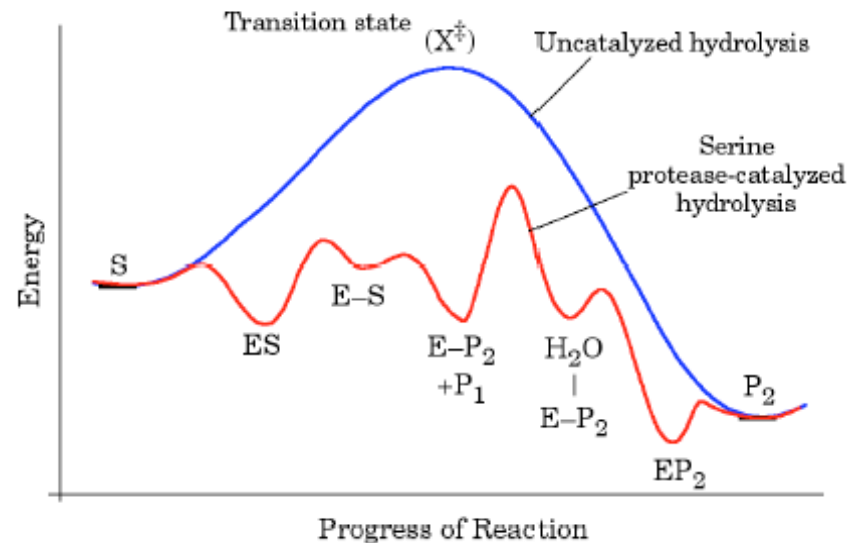
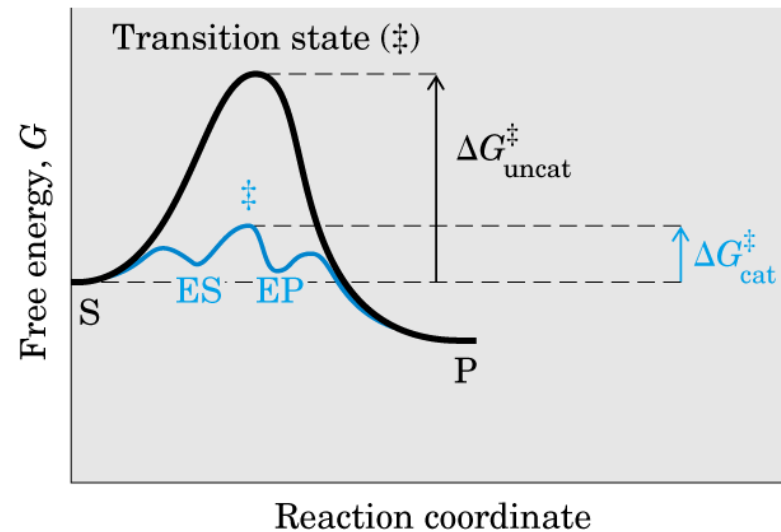
- Enzymes speed up reactions, but have no relation to equilibrium or favorability
- What is an activation energy ($\Delta G^{\circ\ddagger}$) concept?
- Specificity varies (stereoisomers), however, there is none non-specific
- Spontaneous vs. rate!
- What is the transition state?



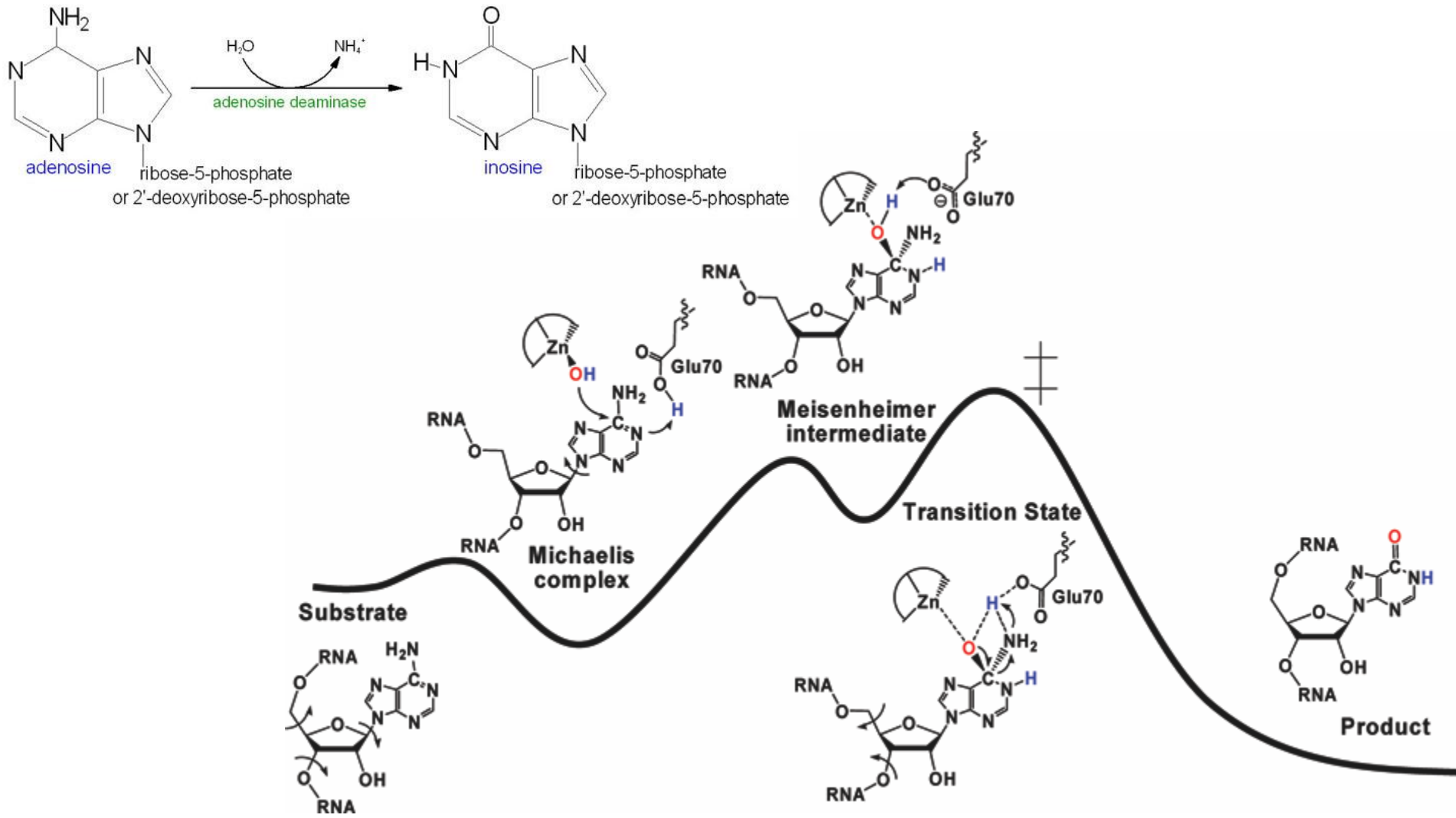
Transition-state complex binds more tightly to the enzyme compared to substrate

Alternative pathways

- Substrates of enzymatic reactions often undergo several transformations when associated with the enzyme and each form has its own free energy value
- Which activation energy?
- Activation energy & final ΔG calculation

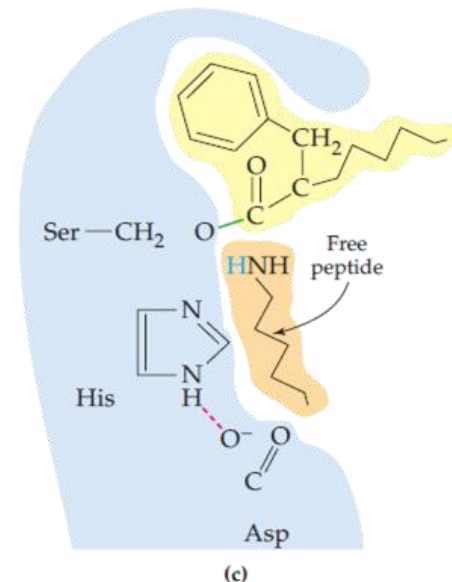
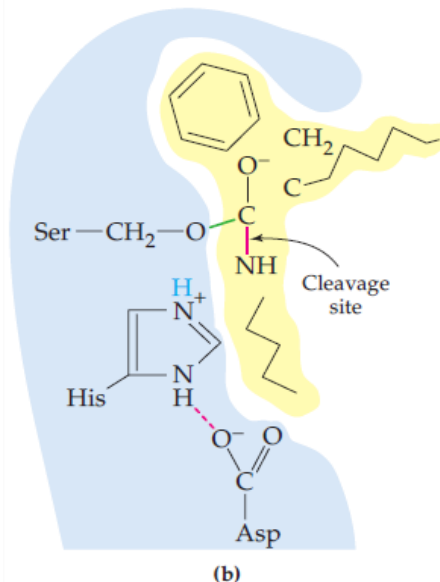
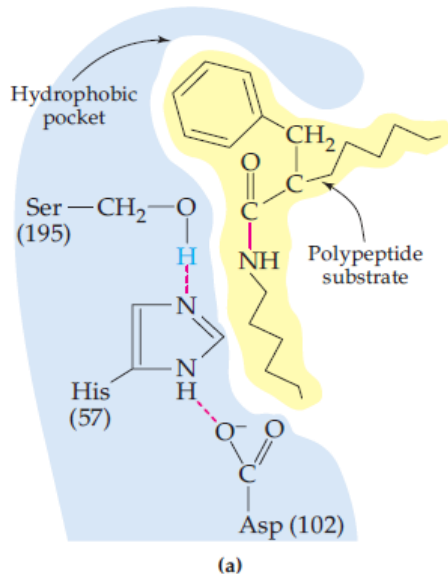


Example: Adenosine Deaminase



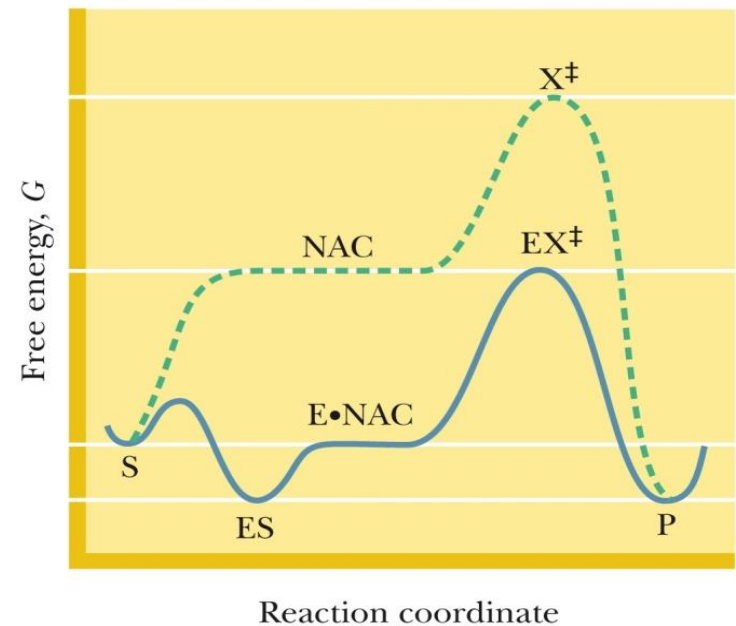
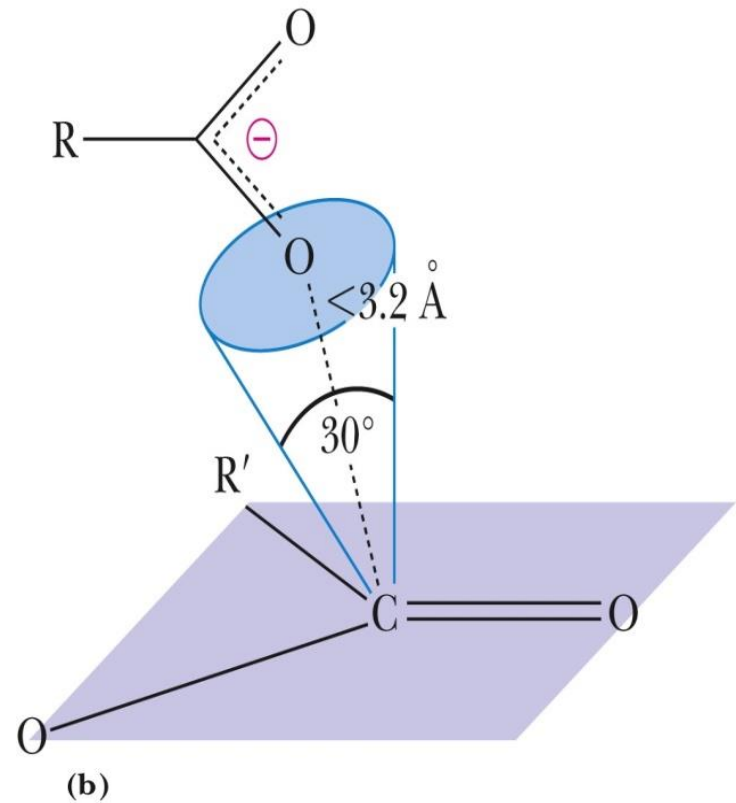
How Do Enzymes Work?

- **Proximity effect:** Bring substrate(s) and catalytic sites together
- **Orientation effect:** Hold substrate(s) at the exact distance and in the exact orientation necessary for reaction
- **Catalytic effect:** Provide acidic, basic, or other types of groups required for catalysis
- **Energy effect:** Lower the energy barrier by inducing strain in bonds in the substrate molecule



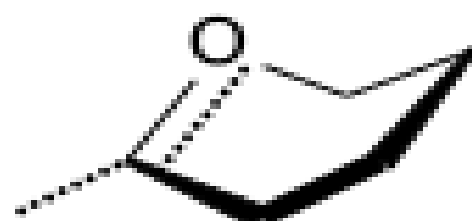
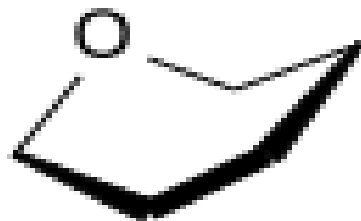
Catalysis by proximity & orientation

- Enzyme-substrate interactions orient reactive groups and bring them into proximity with one another favoring their participation in catalysis
 - Such arrangements have been termed near-attack conformations (NACs)
 - NACs are precursors to reaction transition states



Catalysis by bond strain

- In this form of catalysis, the induced structural rearrangements produce strained substrate bonds reducing the activation energy.

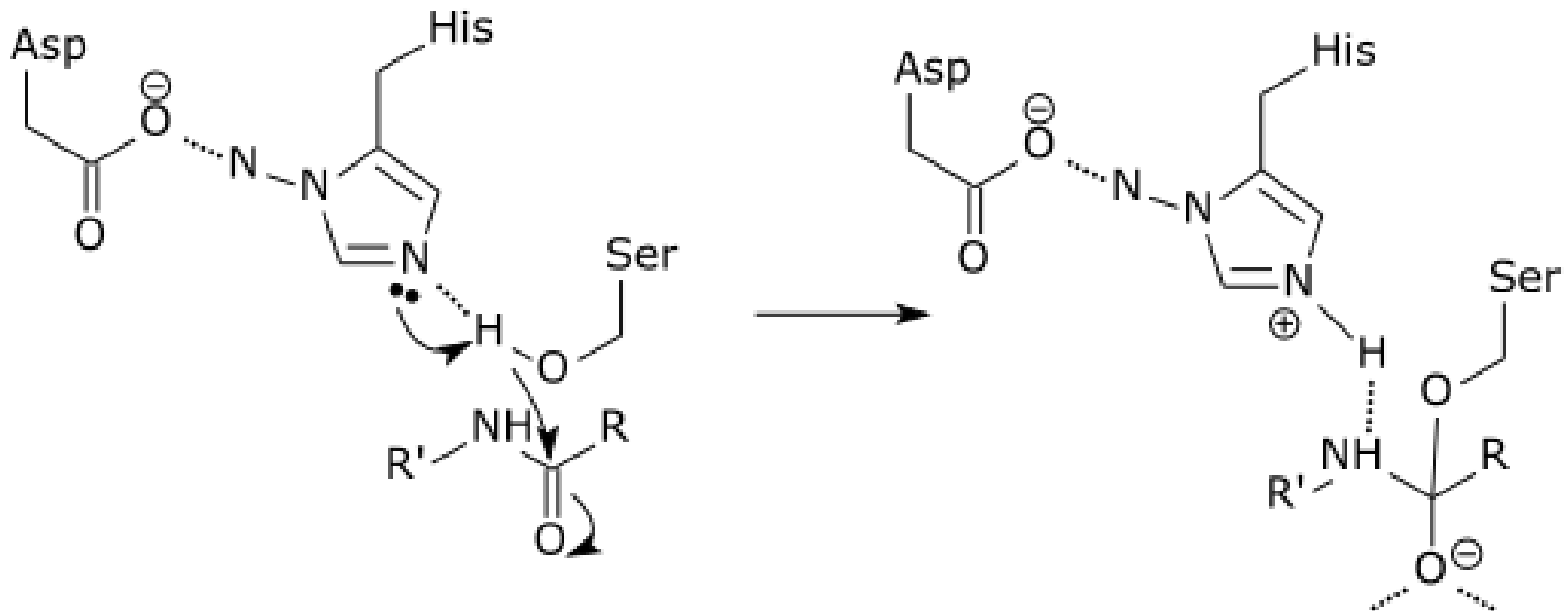


- Example: lysozyme

The substrate, on binding, is distorted from the typical 'chair' hexose ring into the 'sofa' conformation, which is similar in shape to the transition state

Catalysis involving proton donors (acids) & acceptors (bases)

- The R groups act as donors or acceptors of protons
 - Histidine is an excellent proton donor/acceptor at physiological pH
 - Example: serine proteases



Covalent & ionic catalysis

- A covalent intermediate forms between the enzyme or coenzyme and the substrate.
 - Examples of this mechanism is proteolysis by serine proteases, which include both digestive enzymes (trypsin, chymotrypsin, and elastase)

