CHE 349 - Physical Chemistry for Life Sciences

Lecture 13

Concepts

- An **enzyme** is a biological catalyst that can increase the rate of a reaction.
  - The way it works is that it binds to a particular reactant called the substrate and facilitates that reaction by stabilizing its transition state. Once that happens, the enzyme can accelerate the reaction by dramatically reducing the activation energy (E_a)/ free Gibbs energy of activation ($\Delta G^{0\ddagger}$). This will evidently lead to a specific product.
  - Enzymes can be deactivated by a number of substances like oxygen, acids, bases, and metal-ion impurities.
    - It is left unchanged at the end of the reaction
    - NOTE: Most enzymes are proteins
- A **cofactor** is a small molecule that binds to an enzyme.
  - An example of a cofactor is the B family of vitamins
  - A cofactor empowers an enzyme to function at maximal catalytic effectiveness or endurance.

Applications

- An **antibody** is a protein that's synthesized by the immune system in response to a foreign protein that enters the body. It's purpose is to protect the body from that foreign substance.
- An **antigen** is a foreign protein or foreign chemical that enters the body
- A **hapten** is a small molecule that elicit an immune response (e.g. produce antibodies) only when attached to a large carrier such as a protein.
- **REMEMBER**: The way that a catalyst increases the rate of a reaction is by decreasing the free energy of activation.

Transition State ('Eyring') Theory

REMEMBER: A transition state is an unstable species at a free-energy state/maximum
The difference between the free energy of the reactants and the free energy of products is ΔG

$$M + N <--> MN^{\ddagger}$$

$$K^{\ddagger} = \frac{[MN^{\ddagger}]}{[M][N]}$$

$$\frac{d[P]}{dt} = k_1^{\ddagger}[MN^{\ddagger}] \rightarrow \frac{d[P]}{dt} = \frac{k_1 K^{\ddagger}}{k}[M][N]$$

$$k_1^{\ddagger} = \frac{k_b T}{h}$$

$$\Delta G^{\circ\ddagger} = -RTlnk^{\ddagger}$$

$$k = \frac{k_b T}{h} exp(\frac{-\Delta G^{\ddagger}}{RT}) \dashrightarrow \Delta G^{\ddagger} = \Delta H^{\ddagger} - T\Delta S$$

$$[k = \frac{k_b T}{h} exp(\frac{\Delta S^{\ddagger}}{R}) exp(-\frac{\Delta H^{\ddagger}}{RT})]$$

$$\Delta S^{\ddagger} = Rln[\frac{A^{*}k}{k_b T}]$$

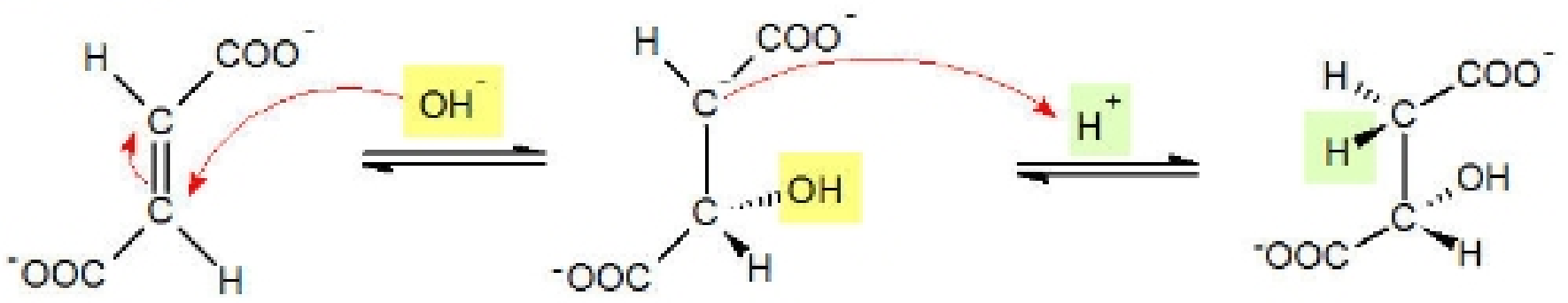
$$\Delta H^{\ddagger} = E_a + R \approx E_a$$

Arrhenius Equation: $k = A * exp(\frac{-E_a}{RT})$

Catalytic constant – turnover number

- The catalytic constant, or turnover number, is defined as the maximum rate $(\frac{M}{s})$ or Ms^{-1} divided by the concentration of enzyme active sites (M). The units for this constant or number are $\frac{1}{s}$ or s^{-1}

Fumarase



Fumarate L-Malate

The image above features the enzyme, fumarase, catalyzing the hydration of fumarate to L-malate with a catalytic constant of $2.5 * 10^3\ s^{-1}$ at 25°. The specific mechanism for this reaction is as follows:

1) The –OH bond will detach from the hydrogen atom and attacks the central carbon atom of fumarate. This will break down the double bond between the central carbon atom and the other carbon atom. The central carbon atom will now have a —OH, —(-)OOC, and a –H substituent attached to it. In addition, that central carbon atom and top carbon atom share a single bond between them.
2) The top carbon atom will then attack the hydride ion, forming a C–H bond. The top carbon atom will now have a —COO(-), a —H, and another —H substituent attached to it.

3) The final product will be L-Malate.

Enzyme kinetics: background and definition

- Biological catalysts
  - DO NOT SHIFT EQUILIBRIUM; THEY JUST ACCELERATE THE REACTION (E.G. THEY INCREASE THE RATE OF THE REACTION
  - They accelerate the reaction by reducing the activation energy E_a/free Gibbs energy of activation ΔG
  - Examples include proteins, RNA ('ribozymes')

Michaelis-Menten (MM) kinetics

To recap:

- Enzymes are catalysts that speed up a reaction

Enzyme catalysis Mechanism:

$E + S \Leftrightarrow ES \Leftrightarrow E + P$

- E: enzyme
- S: substrate
- ES: enzyme-substrate complex
- P: Product

NOTE: Like any other reaction, the enzyme substrate complex can go forwards or backwards (e.g. it can form the product(s), or dissociate back into its substrate and enzyme). However, these kinds of reactions are typically thermodynamically stable, so the dissociation back into a substrate and enzyme almost never happens.

The enzyme catalysis mechanism can be split into 2 steps:

$E + S \Leftrightarrow ES$, R = $k_1[E][S]$

$ES \Leftrightarrow E + P$, R = $k_2[ES]$

Michaelis-Menten (MM) Constant: $V_0 = \frac{V_{max}[S]}{K_M + [S]}$

- K_M: the substrate concentration where the initial reaction speed is one half of the maximum reaction speed
- V_{max}: the maximum reaction speed
- V_0: the initial reaction speed

K_M can be utilized to quantify an enzyme's ability to catalyze reactions

1) A small Km indicates that the enzyme requires only a small amount of substrate to become saturated. Hence, the maximum velocity is reached at relatively low substrate concentrations.
2) A large Km indicates the need for high substrate concentrations to achieve maximum reaction velocity.