Ch. 29 : reaction mechanisms

go over pages 21–26 of my Chapter 19 lecture notes for Chem 1312 since they do a good job going over elementary reactions.

Note: the textbook, on page 1193, discusses in detail when the steady state approx is valid.

29-6 : the Lindemann mechanism.

Consider isomerization or decomposition reactions in the gas phase.

ex: $CH_3NC \rightleftharpoons CH_3CN$

ethyl fluoride $\rightleftharpoons$ HF + ethene

isopropyl ether $\rightleftharpoons$ propene + isopropanol

Only one reactant, so how does the reaction proceed?

Experiments show that the rate law is 1st order at high concentration and 2nd order at low concentration of the reactant. Would like to explain this.

Lindemann proposed a 2nd order bimolecular collisional activation step.

Look at $A \rightleftharpoons B$:

$$A + M \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} A^* + M$$

$$A^* \xrightarrow{k_2} B$$

A^* represents an energized reactant molecule.
M collides with and transfers energy to A.
M can be another reactant molecule or a product molecule, or more likely an inert buffer gas molecule such as N_2 or Ar.

rate of product formation is $\dfrac{d[B]}{dt} = k_2[A^*]$ (†)

Invoke the steady state approx on A^* :

$$\frac{d[A^*]}{dt} = 0 = k_1[A][M] - k_{-1}[A^*][M] - k_2[A^*]$$

Solve for $[A^*] = \dfrac{k_1[M][A]}{k_2 + k_{-1}[M]}$ and sub. in (†)

$$\frac{d[B]}{dt} = -\frac{d[A]}{dt} = \frac{k_1 k_2 [M][A]}{k_2 + k_{-1}[M]} = k_{eff}[A]$$

where $k_{eff} = \dfrac{k_1 k_2 [M]}{k_2 + k_{-1}[M]}$ is pressure-dependent so its not a proper rate constant.

Consider the limiting cases of high and low pressure.

high rate of collisional deactivation > rate of reaction

Why? Lindemann postulated that there must be a time lag between the activating collision and the reaction, so at high concentration the A^* species can be deactivated before it has a chance to react.

This is equivalent to assuming a slow conversion to products from the activated state.

We have $k_{-1}[M][A^*] \gg k_2[A^*] \Longrightarrow k_{-1}[M] \gg k_2$

$$\Rightarrow k_{eff} = \frac{k_1 k_2 [M]}{k_{-1}[M]} = \frac{k_1 k_2}{k_{-1}}$$ and the overall

rate law is $\dfrac{d[B]}{dt} = \dfrac{k_1 k_2 [A]}{k_{-1}}$ 1st order

low rate of conversion to products > deactivation rate

equivalent to assuming slow deactivation

$k_2 \gg k_{-1}[M]$ and $k_{eff} = \dfrac{k_1 k_2 [M]}{k_2} = k_1[M]$

and the overall rate law is $\dfrac{d[B]}{dt} = k_1[M][A]$ 2nd order

Lindemann theory breaks down for 2 main reasons:

(i) the bimolecular step takes no account of the energy dependence of activation; the internal degrees of freedom of the molecule are completely neglected, and the theory consequently underestimates the rate of activation.

(ii) the unimolecular step ($A^* \rightarrow B$) fails to take into account that a unimolecular reaction specifically involves one particular form of molecular motion, eg. rotation about a double bond for cis-trans isomerization.

These are all fixed in RRKM theory.

29-7 : chain reactions

Consider $H_2(g) + Br_2(g) \rightleftharpoons 2HBr(g)$

with experimentally determined rate law

$$\frac{1}{2}\frac{d[HBr]}{dt} = \frac{k[H_2][Br_2]^{1/2}}{1 + k'[HBr][Br_2]^{-1}}$$

The product decreases the reaction rate as it accumulates.
It is thus an inhibitor !

The proposed mechanism, in terms of elementary reactions, is :

$$Br_2 + M \underset{k_{-1} = \text{termination}}{\overset{k_1 = \text{initiation}}{\rightleftharpoons}} 2Br + M$$

$$Br + H_2 \underset{k_{-2} = \text{inhibition}}{\overset{k_2 = \text{propagation}}{\rightleftharpoons}} HBr + H$$

$$H + Br_2 \underset{k_{-3} = \text{inhibition}}{\overset{k_3 = \text{propagation}}{\rightleftharpoons}} HBr + Br$$

The propagation steps are chain reactions involving free radicals.

they each produce what the other one consumes

This is also important in polymerization.

To obtain the experimental rate law from this mechanism, we need to eliminate M, H, and Br from the elementary reactions.

To do this we apply the steady state approx to H and Br, and M ends up canceling out.

Also, we set $k_{-3} = 0$ because it is known this reaction is very slow.

$$\frac{d[H]}{dt} = 0 = k_2[Br][H_2] - k_{-2}[HBr][H] - k_3[H][Br_2]$$

$$\frac{d[Br]}{dt} = 0 = 2k_1[Br_2][M] - 2k_{-1}[Br]^2[M] - k_2[Br][H_2] + k_{-2}[HBr][H] + k_3[H][Br_2]$$

Add these: $0 = k_1[Br_2][M] - k_{-1}[Br]^2[M]$

$$\Rightarrow [Br] = \left(k_1/k_{-1}\right)^{1/2}[Br_2]^{1/2} = K_1^{1/2}[Br_2]^{1/2}.$$

Sub. this into the $\frac{d[H]}{dt} = 0$ expression to get

$$[H] = \frac{k_2[Br][H_2]}{k_{-2}[HBr] + k_3[Br_2]} = \frac{k_2K_1^{1/2}[Br_2]^{1/2}[H_2]}{k_{-2}[HBr] + k_3[Br_2]}$$

Then we use $\frac{d[HBr]}{dt} = k_2[Br][H_2] - k_{-2}[HBr][H] + k_3[H][Br_2]$

with the [H] and [Br] steady state expressions to obtain the observed rate law with $k = k_2K_1^{1/2}$; $k' = k_{-2}/k_3$.

29-9: Michaelis-Menten Mechanism for Enzyme Catalysis

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} E + P$$

assume [P] low so backwards rxn of k_{-2} negligible

E = enzyme ; S = substrate ; P = product ; ES = enzyme-Substrate Complex

$$\text{rate} = \frac{d[P]}{dt} = k_2[ES]$$

during the initial stages of the reaction, before [P] is significant.

Apply the steady state approx to [ES]:

$$\frac{d[ES]}{dt} = 0 = k_1[E][S] - k_{-1}[ES] - k_2[ES]$$

$$\Rightarrow [ES] = \frac{k_1[E][S]}{k_{-1} + k_2}$$

$[E]_0 = [E] + [ES]$ = total amount of E added

$[S]_0 = [S] + [ES] \approx [S]$ substrate in large excess relative to the enzyme.

$$\Rightarrow [ES] = \frac{k_1\left([E]_0 - [ES]\right)[S]}{k_{-1} + k_2} \Rightarrow [ES] + \frac{k_1[ES][S]}{k_{-1} + k_2} = \frac{k_1[E]_0[S]}{k_{-1} + k_2}$$

$$\Rightarrow [ES] = \frac{k_1/(k_{-1} + k_2)\,[E]_0[S]}{1 + k_1/(k_{-1} + k_2)[S]} = \frac{[E]_0}{1 + \frac{k_{-1} + k_2}{k_1} \cdot \frac{1}{[S]}}$$

Thus the rate is $k_2[ES]$

$$= \frac{k_2[E]_0}{1 + \frac{K_m}{[S]}} = \frac{k_2[E]_0[S]}{K_m + [S]}$$

$K_m = \frac{k_{-1} + k_2}{k_1}$ = Michaelis constant

$V_{max} = k_2[E]_0$ = maximum rate

Three special cases:

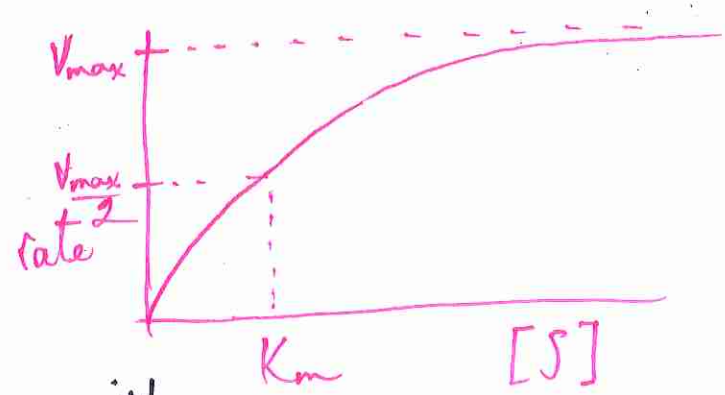
1. Low [S] : $\frac{K_m}{[S]} \gg 1 \Rightarrow \text{rate} \simeq \frac{V_{max}}{K_m}[S] \propto [S]$

2. High [S] : $\frac{K_m}{[S]} \ll 1 \Rightarrow \text{rate} \simeq V_{max}$

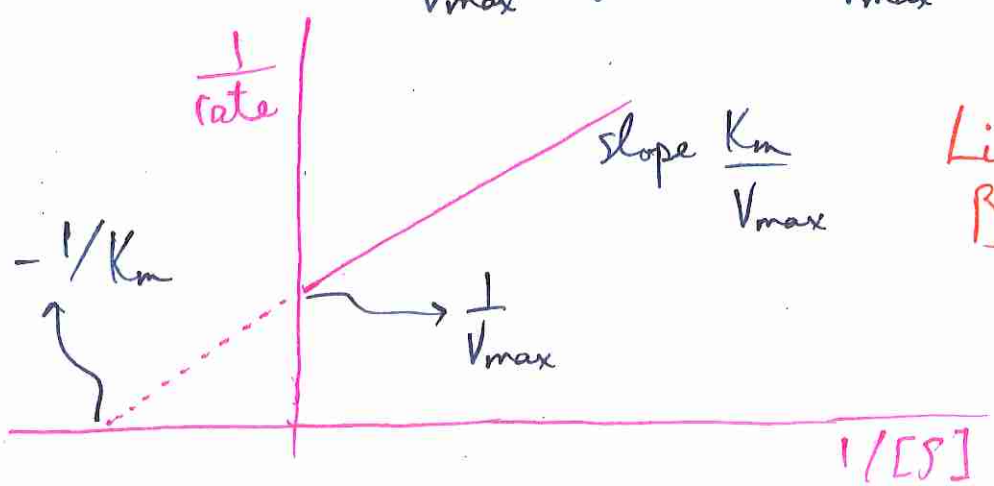
3. $K_m = [S]$: rate $= V_{max}/2$

= substrate conc. at which the reaction rate is half its maximal value.

$$\frac{1}{\text{rate}} = \frac{1}{V_{max}} + \frac{K_m}{V_{max}} \cdot \frac{1}{[S]}$$



So plot $\frac{1}{\text{rate}}$ vs $\frac{1}{[S]}$, straight line with slope $\frac{K_m}{V_{max}}$; y-intercept $\frac{1}{V_{max}}$; x-intercept $-\frac{1}{K_m}$



Lineweaver-Burk plot

Enzyme	k_{cat}/K_M ($s^{-1}M^{-1}$)
Acetylcholinesterase	1.6×10^8
Carbonic anhydrase	8.3×10^7
Catalase	4×10^7
Crotonase	2.8×10^8
Fumarase	1.6×10^8
Triose phosphate isomerase	2.4×10^8
β-Lactamase	1×10^8
Superoxide dismutase	7×10^9

Table 8.7 Substrate preferences of chymotrypsin

$k_{cat} = k_2$

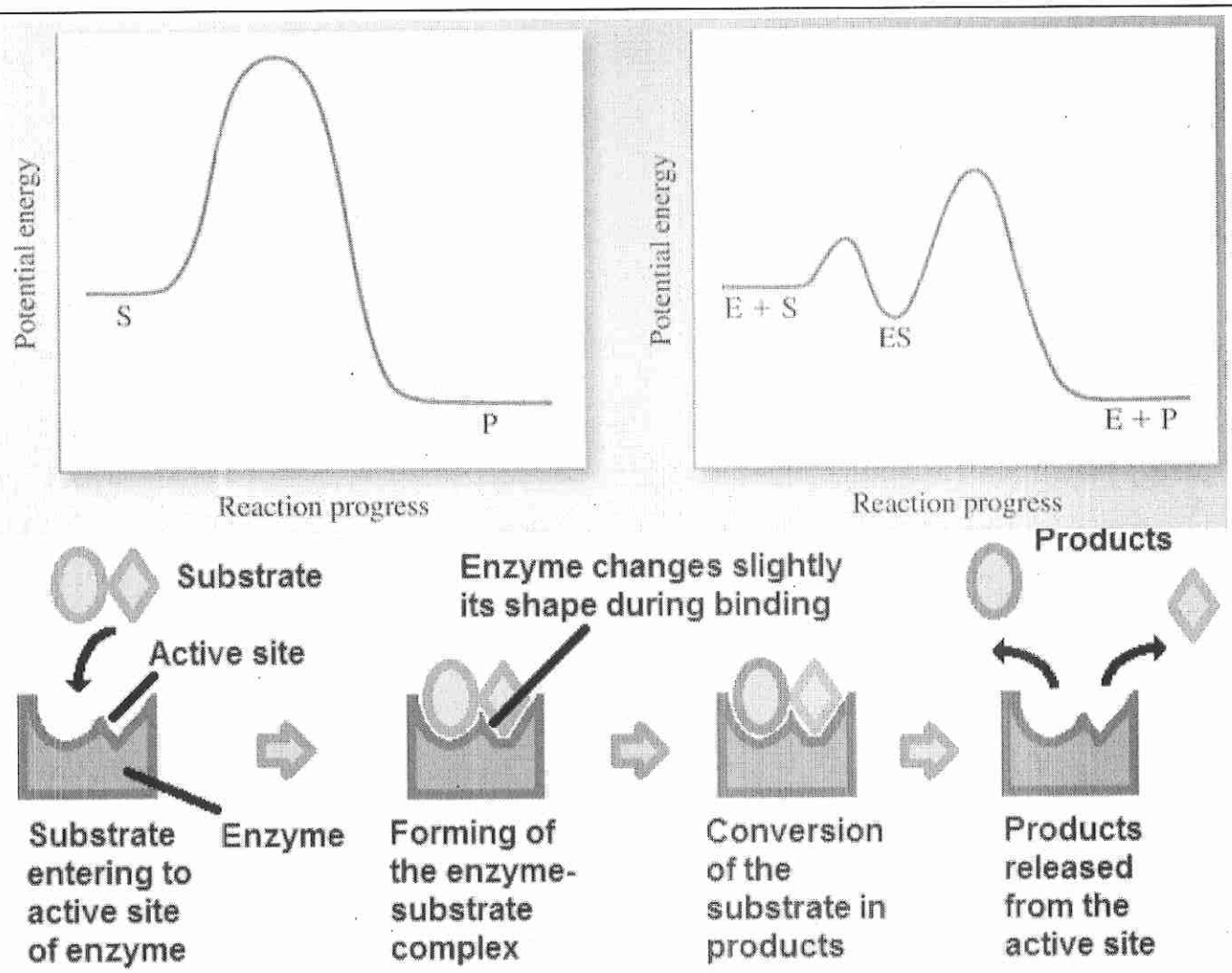
Amino acid in ester	Amino acid side chain	k_{cat}/K_M (s^{-1} M^{-1})
Glycine	—H	1.3×10^{-1}
Valine	—CH(CH_3)$_2$	2.0
Norvaline	—$CH_2CH_2CH_3$	3.6×10^{2}
Norleucine	—$CH_2CH_2CH_2CH_3$	3.0×10^{3}
Phenylalanine	—CH_2—C_6H_5	1.0×10^{5}

Table 8.6 Maximum turnover numbers of some enzymes

Enzyme	Turnover number (per second) = k_2
Carbonic anhydrase	600,000
3-Ketosteroid isomerase	280,000
Acetylcholinesterase	25,000
Penicillinase	2,000
Lactate dehydrogenase	1,000
Chymotrypsin	100
DNA polymerase I	15
Tryptophan synthetase	2
Lysozyme	0.5

Table 8.5 K_M values of some enzymes

Enzyme	Substrate	K_M(μM)
Chymotrypsin	Acetyl-L-tryptophanamide	5000
Lysozyme	Hexa-*N*-acetylglucosamine	6
β-Galactosidase	Lactose	4000
Threonine deaminase	Threonine	5000
Carbonic anhydrase	CO_2	8000
Penicillinase	Benzylpenicillin	50
Pyruvate carboxylase	Pyruvate	400
	HCO_3^-	1000
	ATP	60
Arginine-tRNA synthetase	Arginine	3
	tRNA	0.4
	ATP	300



A biological catalyst (E = enzyme) lowers the activation energy for a chemical reaction.

K_m is the concentration of substrate at which half the active sites are filled. Thus K_m provides a measure of the substrate concentration required for significant catalysis to occur.

When K_m is known, the fraction of sites filled, f_{ES}, is

$$f_{ES} = \frac{[S]}{[S] + K_m}.$$

If we know V_{max} and $[E]_0$ (conc. of active sites), then we can compute $k_2 = \frac{V_{max}}{[E]_0}$ = "turnover" number.

= number of substrate molecules converted into product per unit time when the enzyme is fully ~~satured~~ saturated with substrate.

Each catalyzed reaction takes place in time $1/k_2$.

However, most enzymes are not normally saturated with substrate. This is special case 1, rate $= \frac{V_{max}}{K_m}[S] = \frac{k_2}{K_m}[E]_0[S]$

So $\frac{k_2}{K_m}$ governs the kinetics and gives us a measure of the catalytic efficiency.

$\frac{k_2}{K_m} = \frac{k_2}{k_2 + k_{-1}} \cdot k_1 < k_1$ If $k_2 \gg k_{-1}$, $\frac{k_2}{K_m} = k_1$, and k_1 represents the $E + S$ encounter which is diffusion-limited, so $k_1 < 10^9\ s^{-1} M^{-1}$. Some enzymes reach this value meaning they are "kinetically perfect"