

Lecture 18: Kinetics (continued)

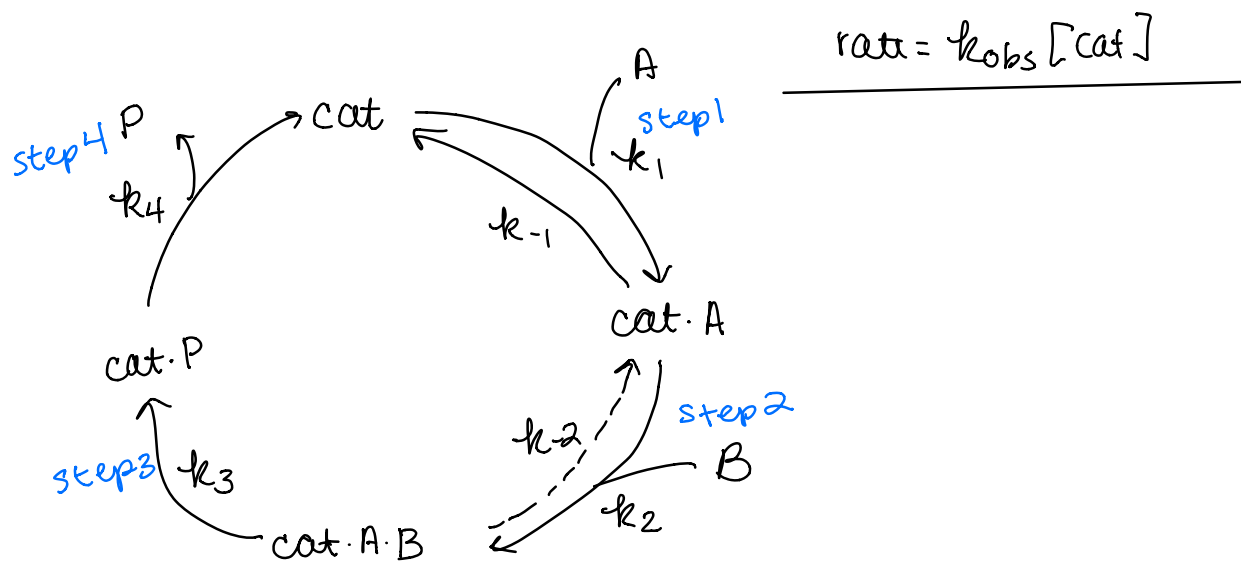
Announcements:

- Problem Set 4 due today
- Problem Set 5 due Thurs, 11/10 (will be posted by Fri morning)
- Midterm 2 on Thurs, 11/17
- No class on Tues, 11/8 (Go vote!)
- Seminar on Wed, 11/9, 4pm, 219 BRL: Prof Bekka Klausen (JHU)

Today:

- A correction from last time
- Kinetics of catalytic cycles (continued)
- Asymmetric catalysis
 - How does it work?
 - Kinetic considerations

Correction from Last Time (Jessica was right)



- 0-order rate dependence on $[A]$ & $[B] \Rightarrow$ In saturated part of the curve for rate vs. $[A]$ & rate vs. $[B] \Rightarrow$ step 1 & step 2 are both fast.

• Possibilities:

(1) Catalyst resting state = $cat \cdot A \cdot B$
Step 3 or 4 is RDS.

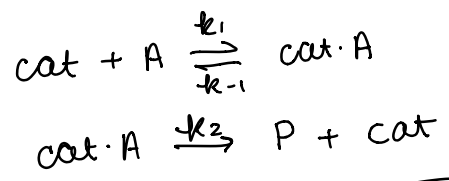
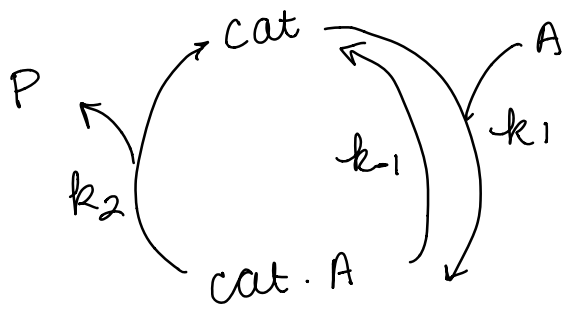
(2) Catalyst resting state = $cat \cdot P$
Step 4 is RDS. (irreversible)

If Step 4 = RDS \Rightarrow irreversible \Rightarrow No inhibition by P.

If Step 3 = RDS \Rightarrow Step 4 may or may not be reversible.

\hookrightarrow Catalyst resting state would have to change to see inhibition by P.

Simplified Catalytic Cycle for Kinetic Analysis:
 very



rate = $k_2 [\text{cat} \cdot \text{A}]$

SSA: $\frac{d[\text{cat} \cdot \text{A}]}{dt} = 0 = k_1 [\text{cat}] [\text{A}] - k_{-1} [\text{cat} \cdot \text{A}] - k_2 [\text{cat} \cdot \text{A}]$

$$[\text{cat} \cdot \text{A}] = \frac{k_1 [\text{cat}] [\text{A}]}{k_{-1} + k_2}$$

$$\text{rate} = \frac{k_1 k_2 [\text{cat}] [\text{A}]}{k_{-1} + k_2}$$

If your catalyst resting state is not all "cat," then...

$$[\text{cat}]_{\text{total}} = [\text{cat}] + [\text{cat} \cdot \text{A}]$$

$$[\text{cat}] = [\text{cat}]_{\text{T}} - [\text{cat} \cdot \text{A}]$$

$$\text{rate} = k_2 [\text{cat} \cdot \text{A}] = \frac{k_1 k_2 [\text{cat}] [\text{A}]}{k_{-1} + k_2}$$

$$k_2 [\text{cat} \cdot \text{A}] = \frac{k_1 k_2 [\text{A}] ([\text{cat}]_{\text{T}} - [\text{cat} \cdot \text{A}])}{k_{-1} + k_2}$$

$$k_2 [\text{cat} \cdot \text{A}] = \frac{k_1 k_2 [\text{A}] [\text{cat}]_{\text{T}} - k_1 k_2 [\text{A}] [\text{cat} \cdot \text{A}]}{k_{-1} + k_2}$$

$$k_2 [\text{cat} \cdot \text{A}] + \frac{k_1 k_2 [\text{A}] [\text{cat} \cdot \text{A}]}{k_{-1} + k_2} = \frac{k_1 k_2 [\text{A}] [\text{cat}]_{\text{T}}}{k_{-1} + k_2}$$

$$k_2 [\text{cat} \cdot \text{A}] \left(1 + \frac{k_1 [\text{A}]}{k_{-1} + k_2} \right) = \frac{k_1 k_2 [\text{A}] [\text{cat}]_{\text{T}}}{k_{-1} + k_2}$$

$$[\text{cat} \cdot \text{A}] = \frac{k_1 [\text{A}] [\text{cat}]_{\text{T}}}{k_{-1} + k_2}$$

$$\left(1 + \frac{k_1 [\text{A}]}{k_{-1} + k_2} \right)$$

$$\text{rate} = k_2 [\text{cat} \cdot \text{A}] = \frac{k_1 k_2 [\text{A}] [\text{cat}]_{\text{T}}}{k_{-1} + k_2}$$

"1+ format"

"naked catalyst"

$$\left(1 + \frac{k_1 [\text{A}]}{k_{-1} + k_2} \right)$$

↖ cat · A

If $[\text{cat}]_T \approx [\text{cat}]$

$$\text{rate} = \frac{k_1 k_2 [\text{A}] [\text{cat}]_T}{k_{-1} + k_2}$$

If $[\text{cat}]_T \approx [\text{cat} \cdot \text{A}]$

$$\text{rate} = \frac{k_1 k_2 [\text{A}] [\text{cat}]_T}{k_{-1} + k_2} = k_2 [\text{cat}]_T$$

1+ General Format :

$$\text{rate} = \frac{C_1 [\text{cat}]_T [\text{A}] [\text{B}]}{1 + C_2 [\text{A}] + C_3 [\text{B}]}$$

} Leads to Product

} where catalyst can be.

We can rearrange...

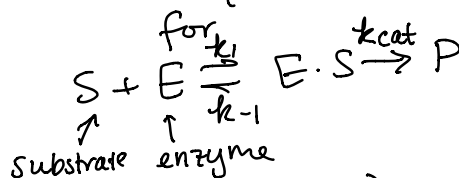
$$\text{rate} = \frac{\frac{k_1 k_2}{k_{-1} + k_2} [A][\text{cat}]_T}{\left(1 + \frac{k_1 [A]}{k_{-1} + k_2}\right)}$$

$$\text{rate} = \frac{k_2 [A][\text{cat}]_T}{\frac{k_{-1} + k_2}{k_1} + \frac{\cancel{k_1} + k_2}{k_1} \cdot \frac{\cancel{k_1} [A]}{\cancel{k_{-1} + k_2}}}$$

$$\text{rate} = \frac{k_2 [A][\text{cat}]_T}{\frac{k_{-1} + k_2}{k_1} + [A]} \approx \frac{k_{\text{cat}} [E][S]}{K_M + [S]}$$

Michaelis-Menton Equation

Michaelis-Menton:



k_{cat} = rate constant for catalyst (fast possibility)

K_M = Michaelis constant = $\frac{k_{-1}}{k_1}$ = Dissociation constant for E.S

Limiting Scenarios:

1) $[S] \gg K_M$

$$\text{rate} = \frac{k_{\text{cat}} [E][S]}{[S]} = k_{\text{cat}} [E]$$

$$\text{rate} = \frac{k_{\text{cat}} [E][S]}{K_M + [S]}$$

= V_{max} = fastest enzyme can go.

2) $[S] \ll K_M$

$$\text{rate} = \frac{k_{\text{cat}} [E][S]}{K_M} \Rightarrow$$

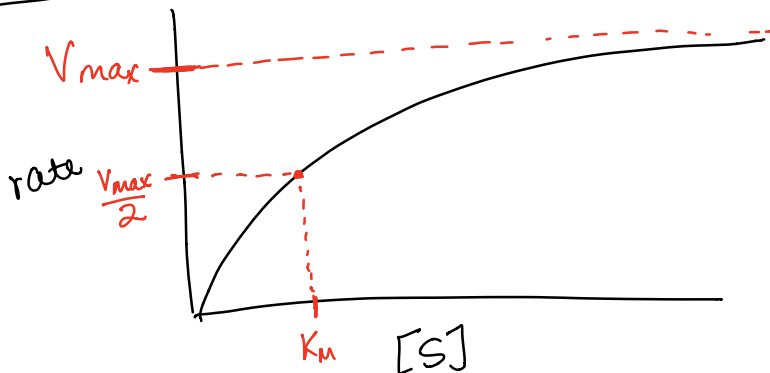
$\frac{k_{\text{cat}}}{K_M}$ } Measure of catalyst efficiency

$\sim 10^8 - 10^{10}$ for a perfect catalyst (diffusion controlled)

3) $[S] = K_M$

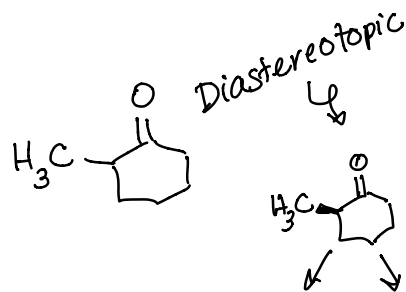
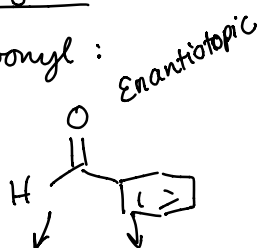
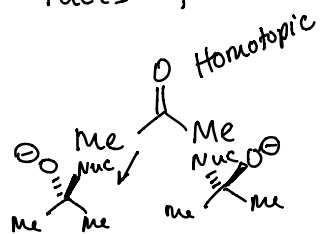
$$\text{rate} = \frac{k_{\text{cat}} [E][S]}{2[S]} = \frac{1}{2} V_{\text{max}}$$

MM Plots:



Asymmetric Catalysis

Faces of a Carbonyl:

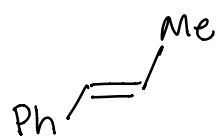


Homotopic = same

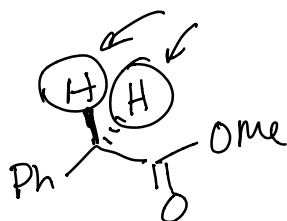
Enantiotopic = lead to enantiomers

Diastereotopic = lead to diastereomers

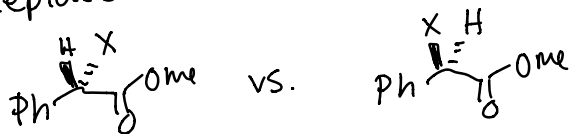
Other enantiotopic things



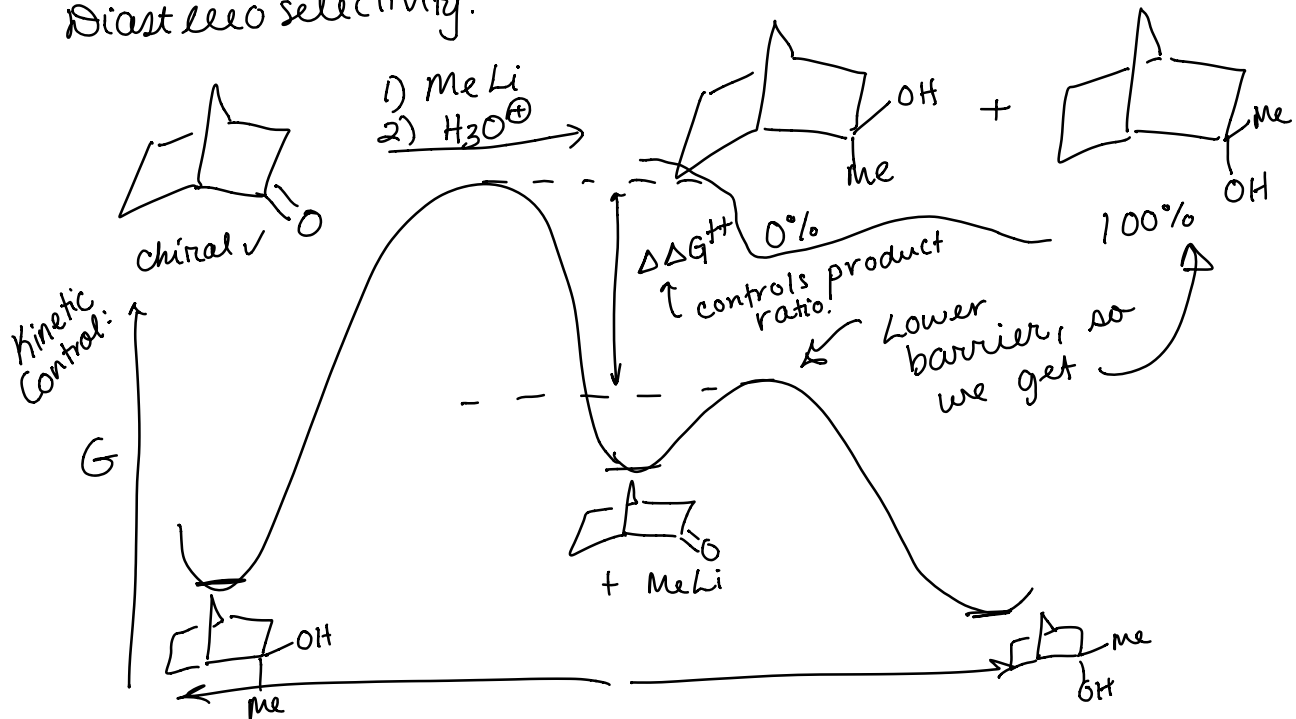
faces of π -systems



Replace each w/ X

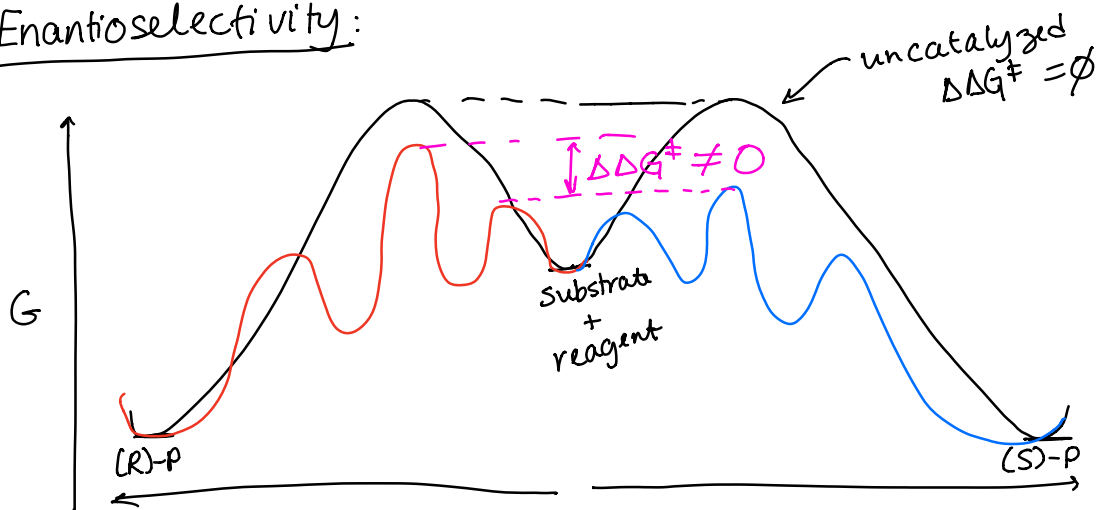


Diastereo selectivity:



(Thermodynamic Control \Rightarrow Must be reversible or some other way to interconvert products)

Enantioselectivity:



Enantioselective Catalyst must be under Kinetic Control.

$\Delta\Delta G^\ddagger$ that determines ratio of P's.

↓
ee or er

ΔG° or $\Delta\Delta G^\ddagger$
1.4 kcal/mol \Rightarrow factor of 10 K_{eq} $\hat{=}$ er

temp (°C)	$\Delta\Delta G^\ddagger$	
	90% ee	99% ee
-78	1.1	2.1
25	1.7	3.1
100	2.2	3.9

Why are energy barriers different?

- 1) Chiral Catalyst
- 2) Stereochemical communication

stabilizing or destabilizing
 covalent bonds $\pi-\pi$
 ionic bonds hydrophobic
 electrostatic steric \times
 H-bonding \uparrow
 dipole-dipole

For chiral recognition:

≥ 3 simultaneous interactions
 ≥ 1 must be "stereochemically dependent"

↓
 (3D)