

① LECTURE 10: KINETICS *Reading: A&D, Ch 7-8

Announcements:

Midterm 1: AVG 53%
HIGH 94%

≥ 70% A

≥ 60% B+

≥ 40% B

PS #5: due Tues 10/13

Seminar: Vlad Grushin
Wed @ 4pm

② PREVIOUSLY, Thermodynamics to predict position of equilibrium. But most organic rxns involve irreversible or kinetically controlled steps.

THERMODYNAMICS is not enough. We need kinetics to fully analyze a mechanism.

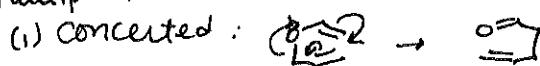
Remember:
Mech can never be proven, but it can be disproven.
Good mech's lead to rational predictions.

③ ENERGY SURFACES

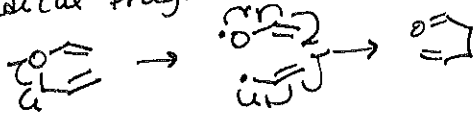
Consider: Claisen Rearrangement



Multiple Possible Mechanisms:



(2) Radical Fragmentation:



(3) Ionic Fragmentation:

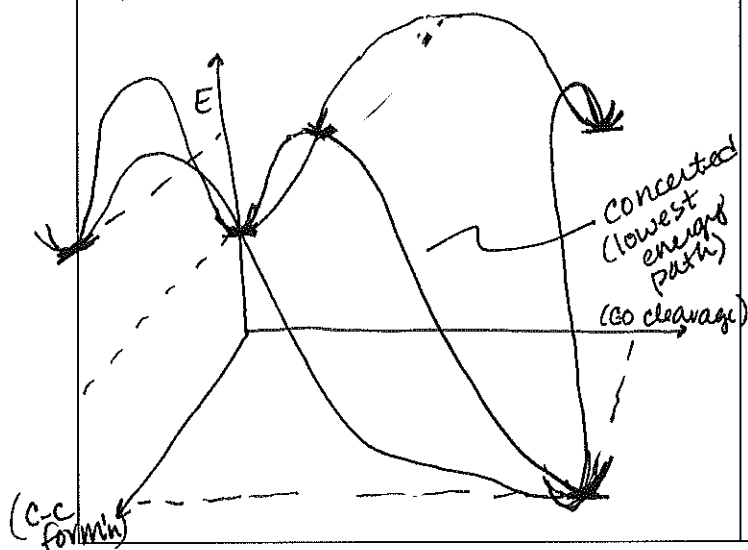


④

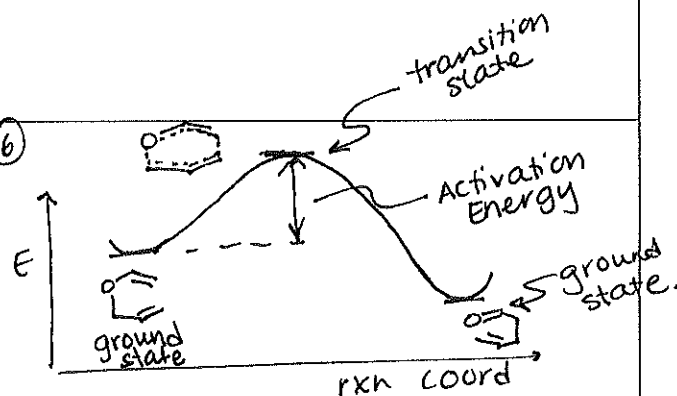
(4) Bond forms 1st



⑤ All these pathways can be put on an energy surface...



⑥



"Ground States" = local minima

$$\frac{dE}{dx} = 0$$

$$\frac{d^2E}{dx^2} > 0$$

Starting Materials
Intermediates
Products

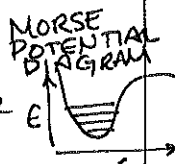
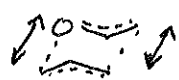
⑦ "Transition States" = Saddle points
Minimum in every direction
but 1.

$$dE/dx = 0$$

$$d^2E/dx^2 < 0$$

lifetime = 1 molecular vibration
corresponding to the
rxn coordinate.

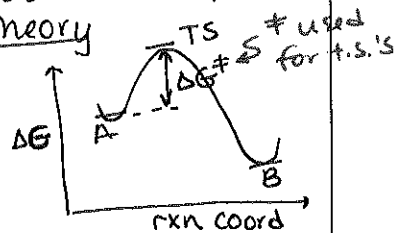
Remember → All structures have
quantized energy states



⑧ How can we get information
about transition states & intermediates
that are not observable?

Transition State Theory

Simplest Case:



rate of form'n of B

$$\text{rate} = k[A] = k^\ddagger [TS]$$

$$k^\ddagger \approx \frac{k_B T}{h} \uparrow \text{temp.}$$

$$\frac{k_B}{h} = 2.083 \times 10^{10} \text{ s}^{-1} \text{ K}^{-1}$$

$k^\ddagger \approx$ inefficiency
in going over ts. ≈ 1

Assuming we can
get to TS
 $k^\ddagger =$ rate ~~constant~~
for fastest possible
rxn, one w/ no
barrier = 1 vibration.

$$\frac{k_B}{h} T @ 298 \text{ K} = 6 \times 10^{12} \text{ s}^{-1} \approx 10^{13}$$

↑
Rate of molecular
vibration.

⑨ We can describe "equilibrium"
between A & TS...

$$K^\ddagger = \frac{[TS]}{[A]}$$

Recall: $K_{eq} = e^{-\Delta G^\ddagger / RT}$

$$[TS] = K^\ddagger [A]$$

$$[TS] = e^{-\Delta G^\ddagger / RT} [A]$$

$$\text{So... } k[A] = \frac{k_B T}{h} e^{-\Delta G^\ddagger / RT} [A]$$

$$k = \frac{k_B T}{h} e^{-\Delta G^\ddagger / RT}$$

→ EYRING EQUATION
- defines relationship between rate
& ΔG^\ddagger !!

⑩ In Organic Synthesis,
 $\Delta G^\ddagger < 25 \text{ kcal/mol}$
(for useful rxns)
→ See handout.

→ If we measure rate, we learn
about Gibbs free energy of transition
state.

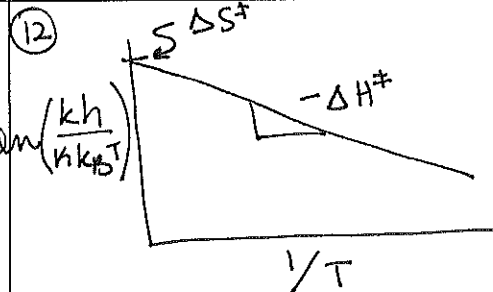
⑪ Recall: $\Delta G^\circ = \Delta H^\circ - T \Delta S^\circ$
Also true for t.s.:
 $\Delta G^\ddagger = \Delta H^\ddagger - T \Delta S^\ddagger$

$$\text{So... } k = \frac{k_B T}{h} e^{-\Delta G^\ddagger / RT} =$$

$$= \frac{k_B T}{h} e^{-\Delta H^\ddagger / RT} e^{\Delta S^\ddagger / R}$$

$$\ln\left(\frac{kh}{k_B T}\right) = \frac{-\Delta H^\ddagger}{RT} + \frac{\Delta S^\ddagger}{R}$$

Not only can we figure out ΔG^\ddagger ,
but also ΔH^\ddagger & ΔS^\ddagger by determining
the reaction rate.



So we know if transition
state has more or less
enthalpy & entropy than
ground state.

Enthalpy control: ΔH^\ddagger is major contributor
to ΔG^\ddagger

Entropy control: ΔS^\ddagger is major contributor
to ΔG^\ddagger

↳ changes w/ temperature!!

⑬ Interpretation of ΔS^\ddagger

If $\Delta S^\ddagger < 0$, then t.s. is more ordered than ground state.

ex: S_N2 CH3I + [CN-] -> CH3CN $\Delta S^\ddagger = -30 \text{ eu}$

NC...H...I \leftarrow highly ordered t.s.

$Nu^- + \triangle \rightarrow Nu-O^-$ $\Delta S^\ddagger = -8 \text{ eu}$

↳ entropy is not as negative b/c epoxide is opening.

⑭ If $\Delta S^\ddagger > 0$, then t.s. is more disordered than SM.

ex: R-O-O-R -> 2R-O- $\Delta S^\ddagger = +10 \text{ eu}$

usually, $-30 \text{ eu} < \Delta S^\ddagger < +10 \text{ eu}$

Some exceptions if t.s. involves 3 species coming together.

⑮ Everything so far... 1 mechanism (1 elementary step) at play.

Arrhenius Equation:

(macroscopic rate constants \rightarrow maybe ≥ 1 mech at play)

$k = A e^{(-E_a/RT)}$

related to ΔH^\ddagger

related to entropy (ΔS^\ddagger)

⑯ More about rxn coordinates... We can determine (or try to determine) ΔG^\ddagger , ΔH^\ddagger , ΔS^\ddagger ...

How else can we think about transition states?

HAMMOND POSTULATE

Consider:

Endothermic step: "product-like" t.s.

Exothermic step: "starting material-like" t.s.

⑰ ex: Electrophilic Aromatic Substitution

c1ccccc1 + [E+] -> [c1ccccc1E] Endothermic

"product-like"

So can think about regioselectivity in terms of stabilities of cationic intermediates.

⑱ In reality, most transformations have > 1 elementary step... & may have > 1 mechanistic pathway occurring.

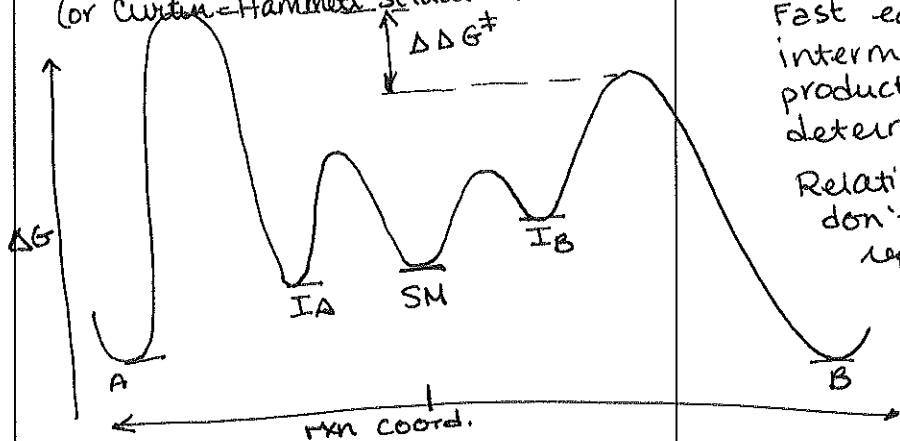
Experimentally determine rate & rate dependence on each reactant to understand which steps are fast or slow & what is involved in rds transition structure...

A, X, Y are involved, but not Z .

MORE ON KINETIC STUDIES NEXT TIME.

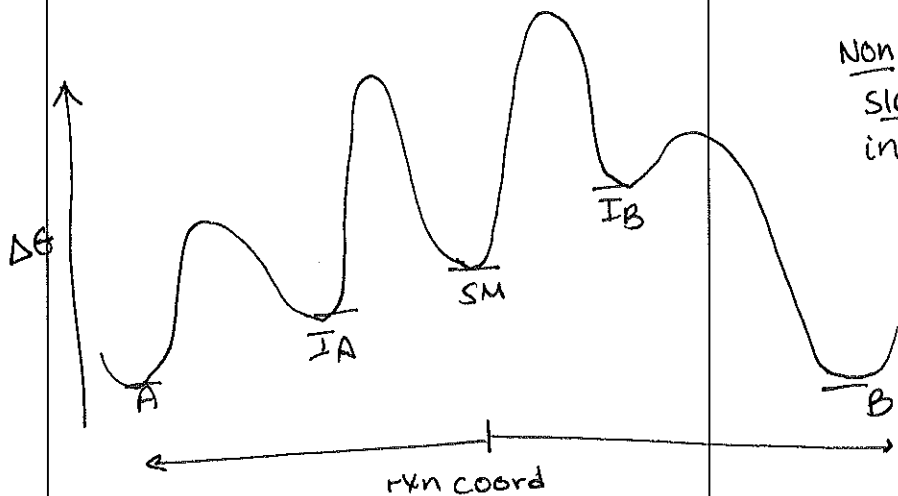
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Curtin-Hammett Principle
(or Curtin-Hammett Situation)



(Kinetic Control)
Fast equilibration of intermediates, so selectivity product formation is determined by $\Delta\Delta G^\ddagger$.
Relative energies of $IA \& IB$ don't matter/are not reflected in A:B ratio.

20 Alternative:



Non - Curtin-Hammett
Slow Equilibration of intermediates.

21 Famous Example: Asym Hydrogenation (Halpern Science 1982, 217, 401)

