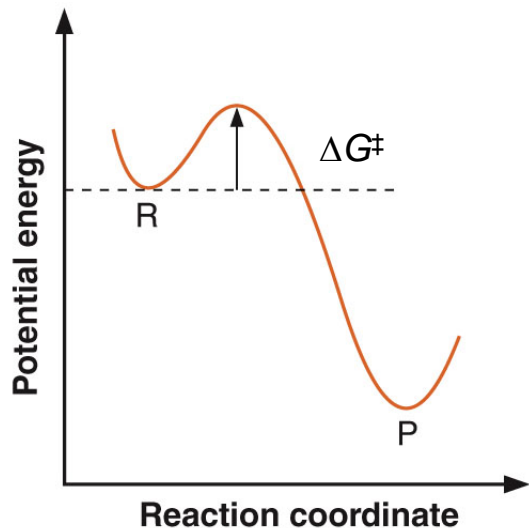


Transition States in Multistep Kinetics

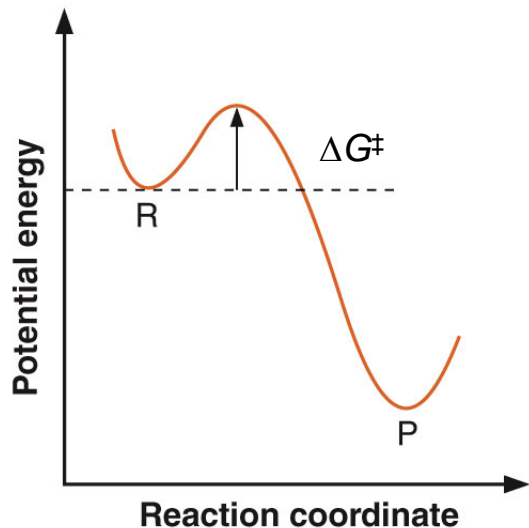


$$k_{\text{rxn}} = \frac{k_B T}{h} e^{-\Delta G^\ddagger / RT}$$

When we determine ΔG^\ddagger , what are we actually measuring?

For simple kinetics, answer is easy.

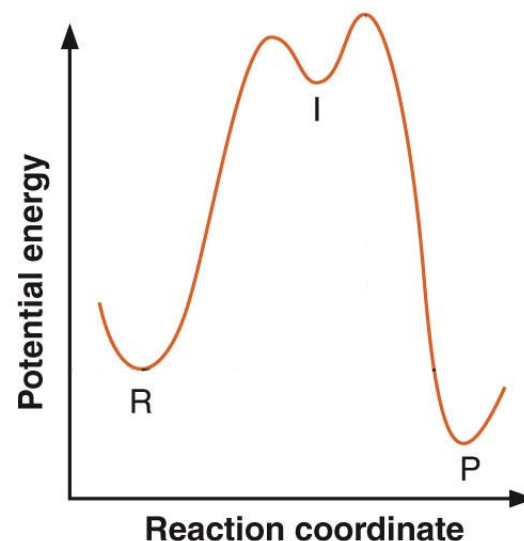
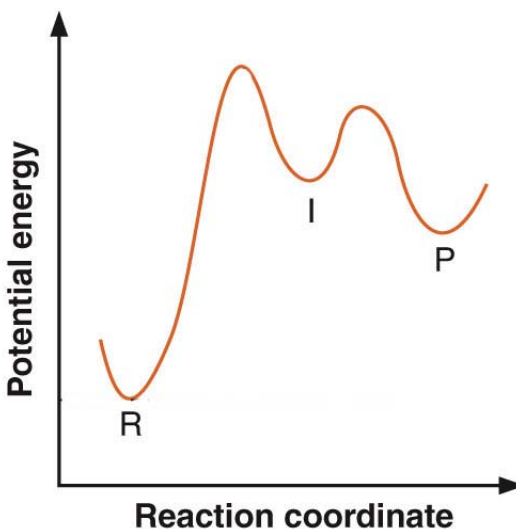
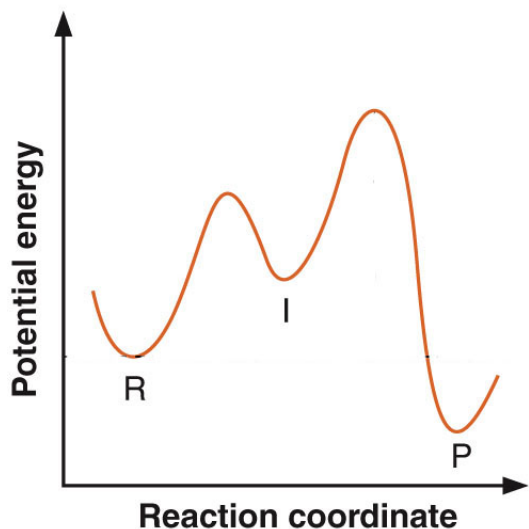
Transition States in Multistep Kinetics



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

When we determine ΔG^\ddagger , what are we actually measuring?

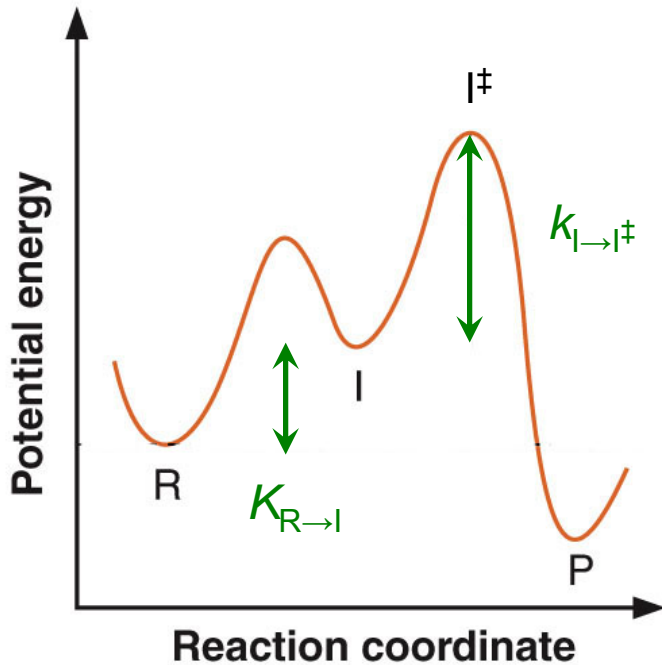
But what about multistep reactions?
Where do we draw ΔG^\ddagger ?



Transition States in Multistep Kinetics

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

If we assume pre-equilibrium between R and I,



$$\frac{\partial [P]}{\partial t} = k_{I \rightarrow I^\ddagger} [I]$$

$$= k_{I \rightarrow I^\ddagger} K_{R \rightarrow I} [R] \quad \left(K_{R \rightarrow I} = \frac{[I]}{[R]} \right)$$

Eyring (TST)

K_{eq}

$$= \left(\frac{k_B T}{h} e^{-\Delta G_{I \rightarrow I^\ddagger} / RT} \right) \left(e^{-\Delta G^0_{R \rightarrow I} / RT} \right) [R]$$

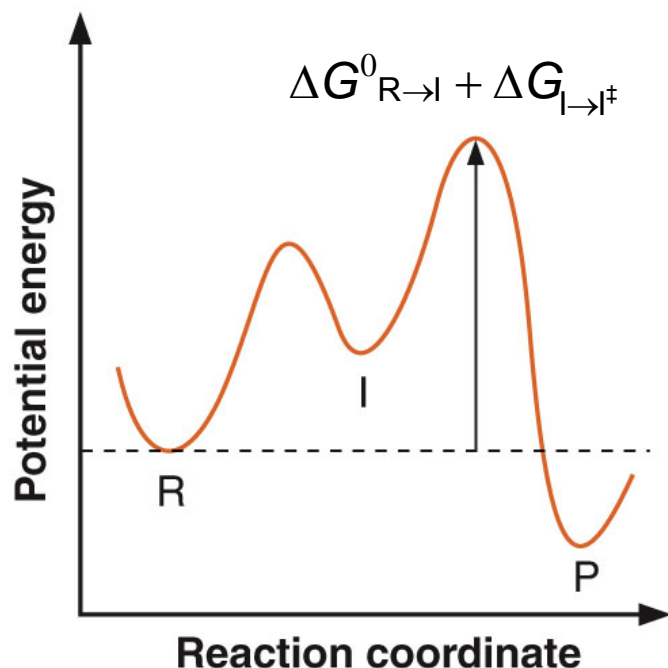
$$= \frac{k_B T}{h} \left(e^{-\{\Delta G^0_{R \rightarrow I} + \Delta G_{I \rightarrow I^\ddagger}\} / RT} \right) [R]$$

Transition States in Multistep Kinetics

$$k_{\text{rxn}} = \frac{k_{\text{B}}T}{h} e^{-\Delta G^{\ddagger} / RT}$$

If we assume pre-equilibrium between R and I,

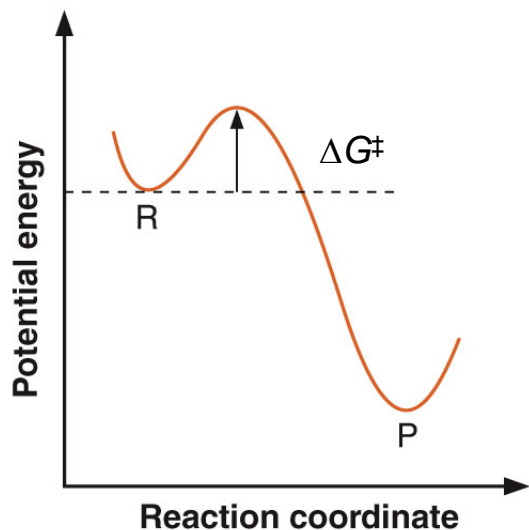
$$k_{\text{obs}} = \frac{k_{\text{B}}T}{h} \left(e^{-\{\Delta G^{\circ}_{\text{R} \rightarrow \text{I}} + \Delta G_{\text{I} \rightarrow \text{I}^{\ddagger}}\} / RT} \right)$$



Conclusions: “Rate-determining” transition state is the one that’s highest in energy.

Reaction barrier is between starting material and highest-energy transition state.

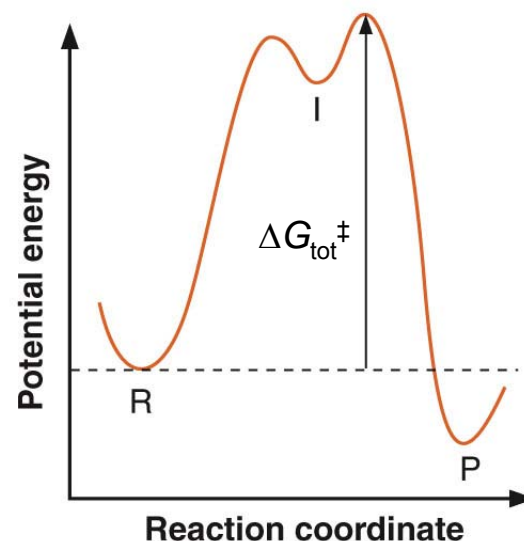
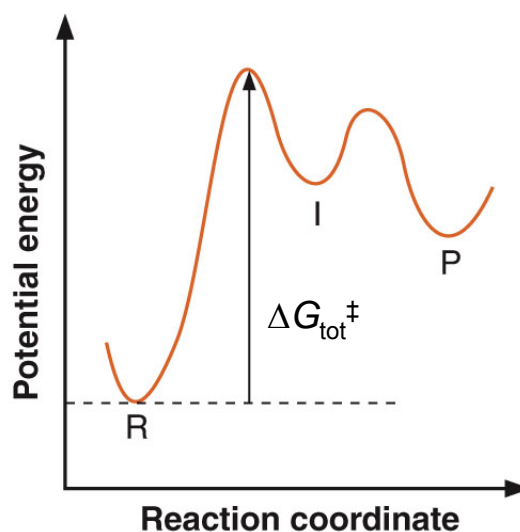
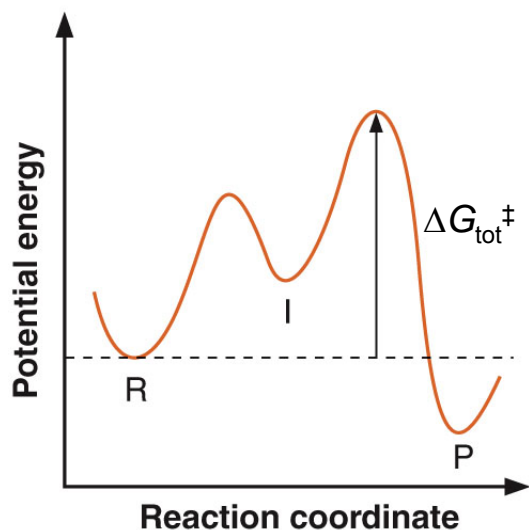
Transition States in Multistep Kinetics



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

When we determine ΔG^\ddagger , what are we actually measuring?

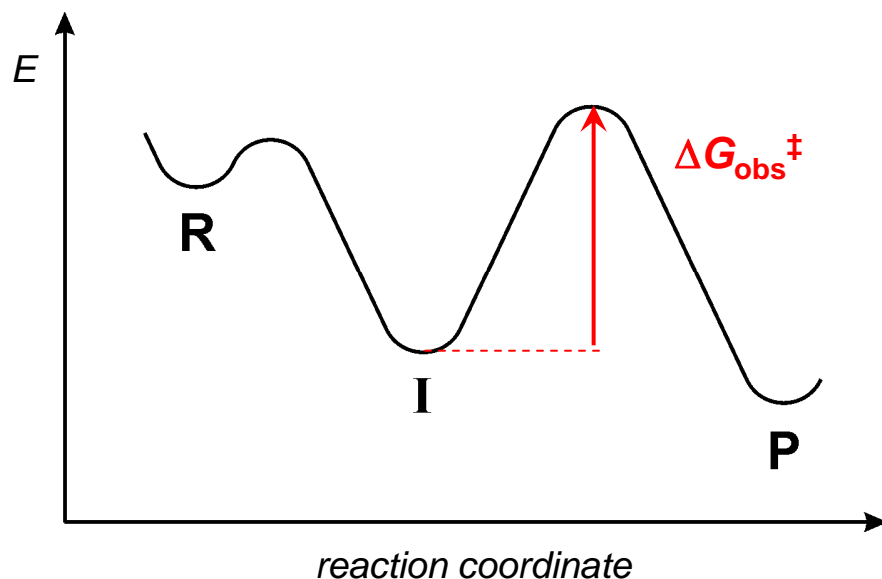
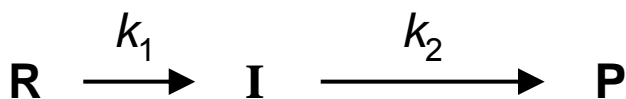
Reaction barrier is between starting material and highest-energy transition state.



Transition States in Multistep Kinetics

Exception to “Reaction barrier is between starting material and highest-energy transition state.”:

Uncoupled forward reactions.



What is the rate of this reaction?

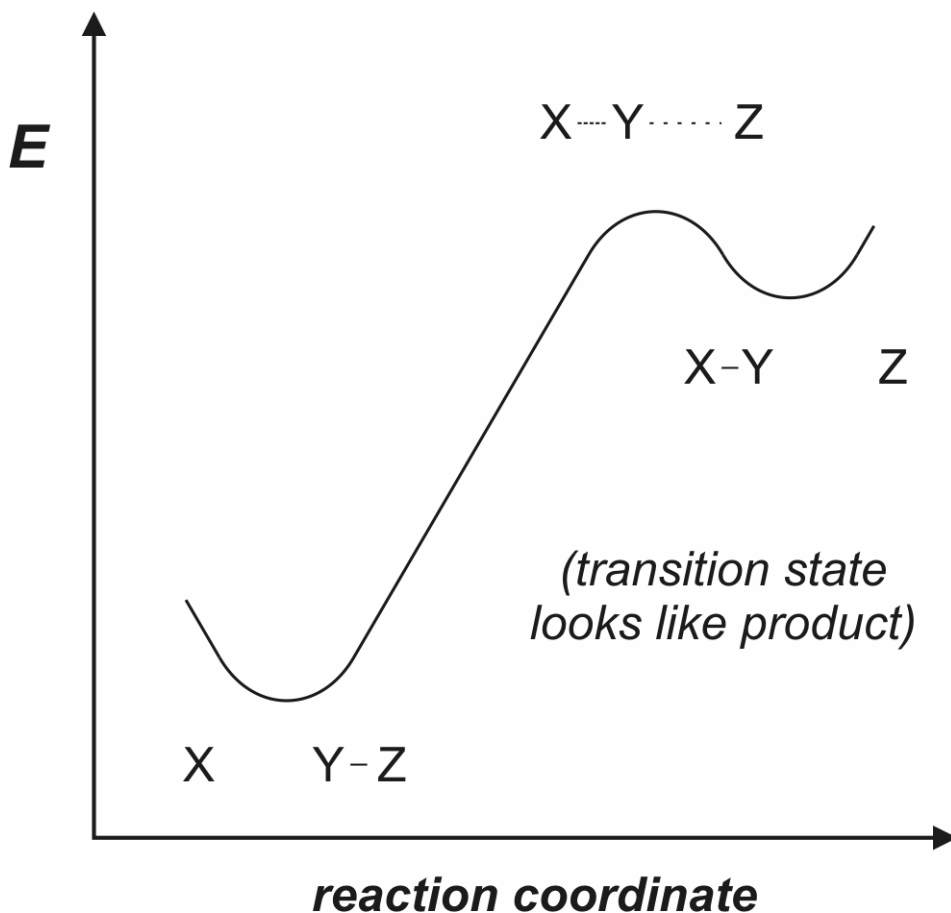
Really, this is two reactions.
First reaction is complete before
second one even gets started.

So, $k_{\text{obs}} \approx k_2$.

Good way to think about it: Imagine I is your new starting material.

Seeing Trends in Kinetics: The Hammond Postulate

Ground-state thermodynamics *do* correlate with transition-state kinetics.

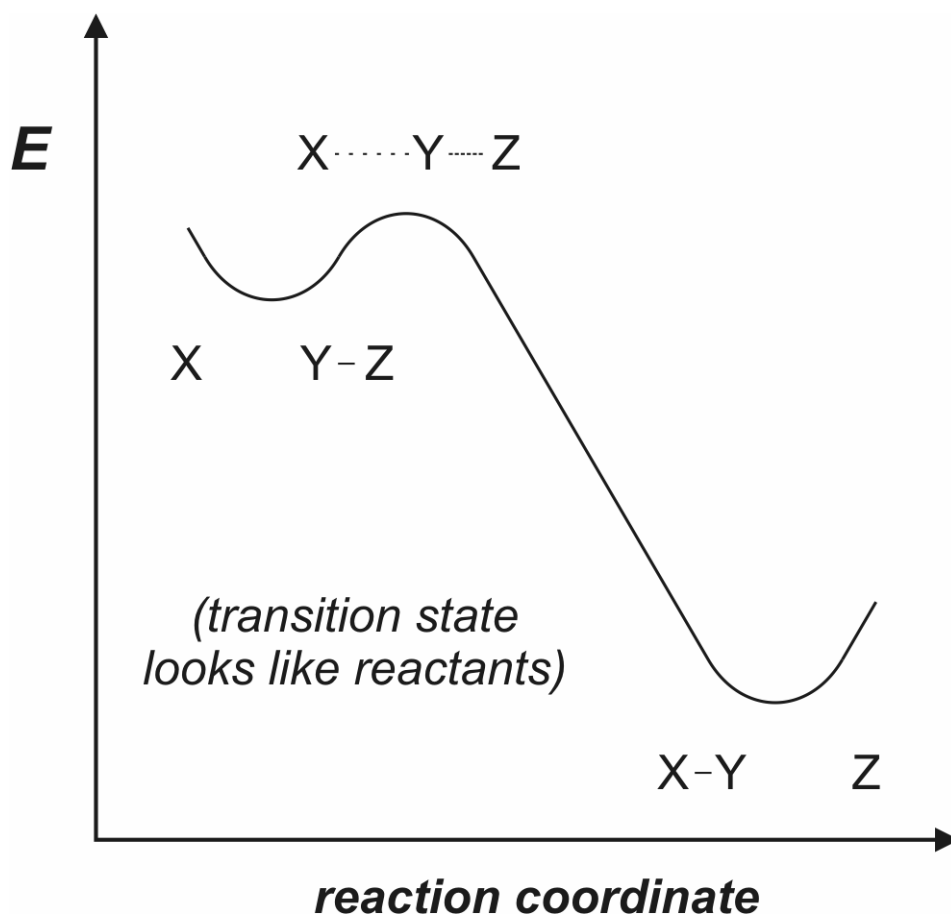


In general, endothermic reactions have transition states that resemble products...

If $\Delta G^{\circ} \gg 0$,
then ΔG^{\ddagger} large,
"late" TS.

Hammond Postulate

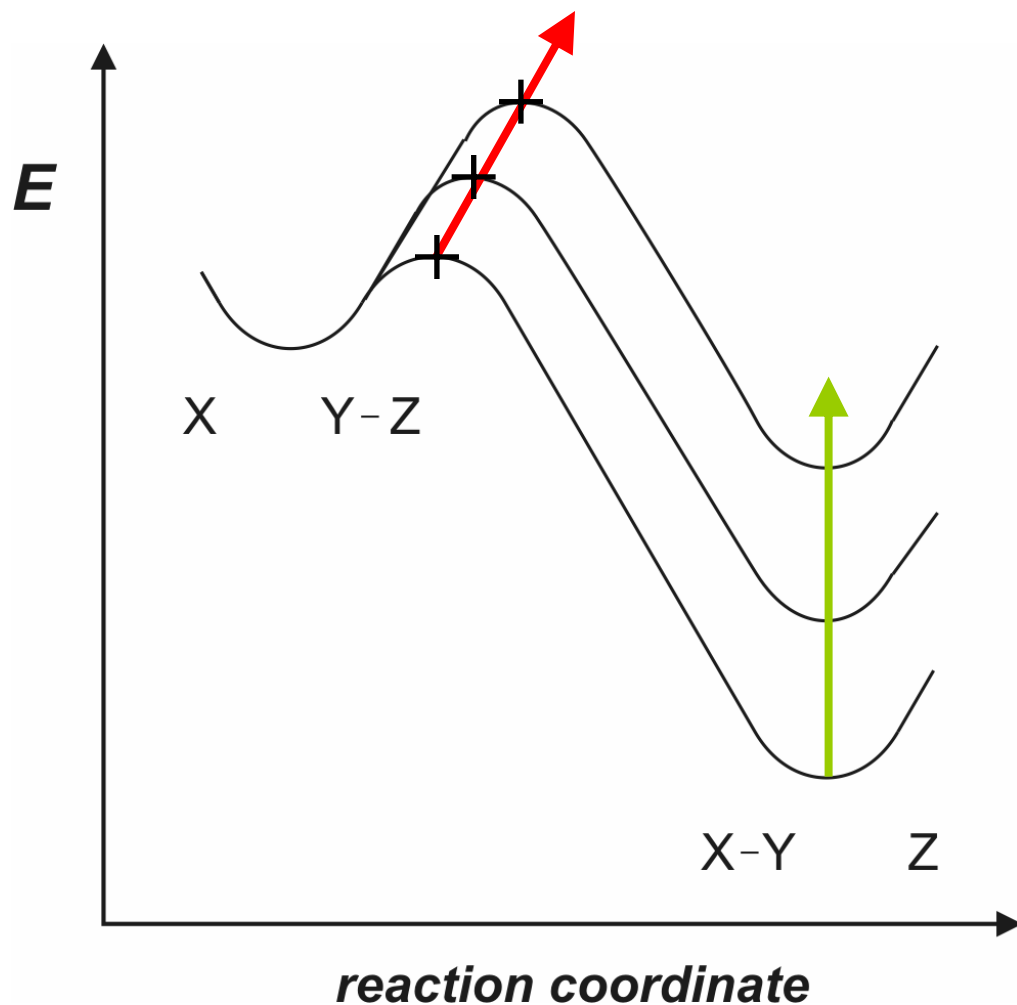
Ground-state thermodynamics do correlate with transition-state kinetics.



...and exothermic reactions have transition states that resemble reactants.

If $\Delta G^\circ \ll 0$,
then ΔG^\ddagger small,
"early" TS.

Hammond Postulate

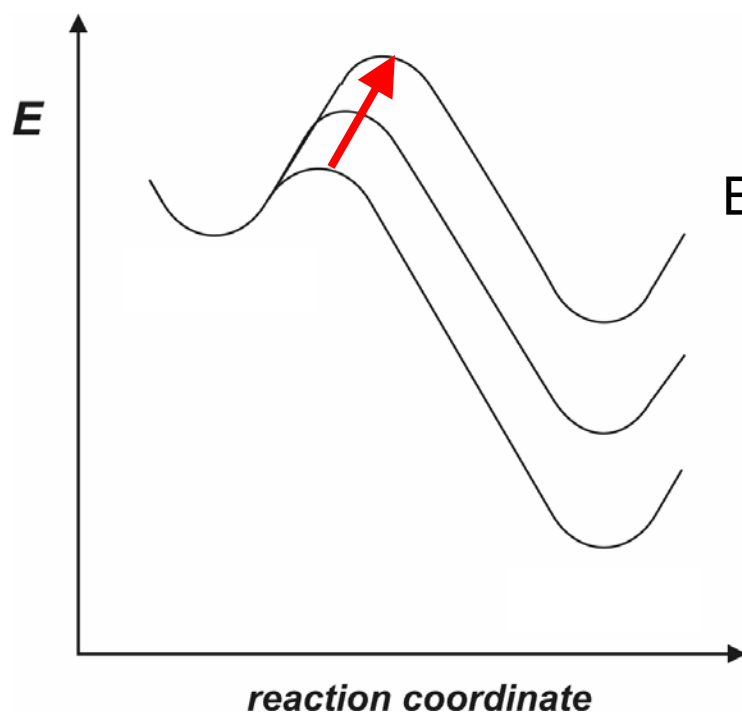
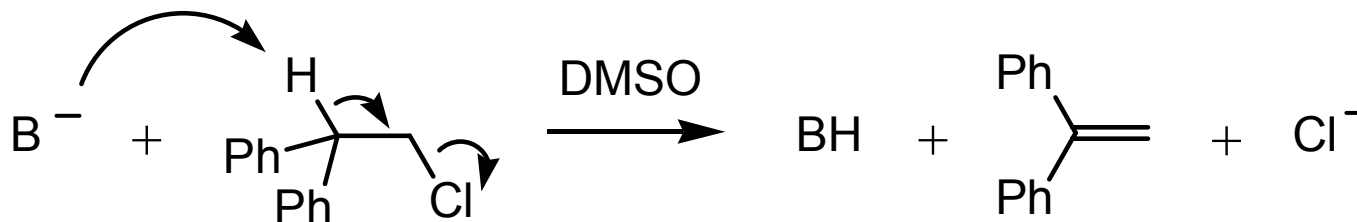


Variation in ΔG°
shows up in ΔG^\ddagger .

*(So, the less exothermic
the reaction is, the later
and higher-energy the
transition state.)*

Only holds for series of
reactions with same
mechanism.

Hammond Postulate Example: E2 Elimination

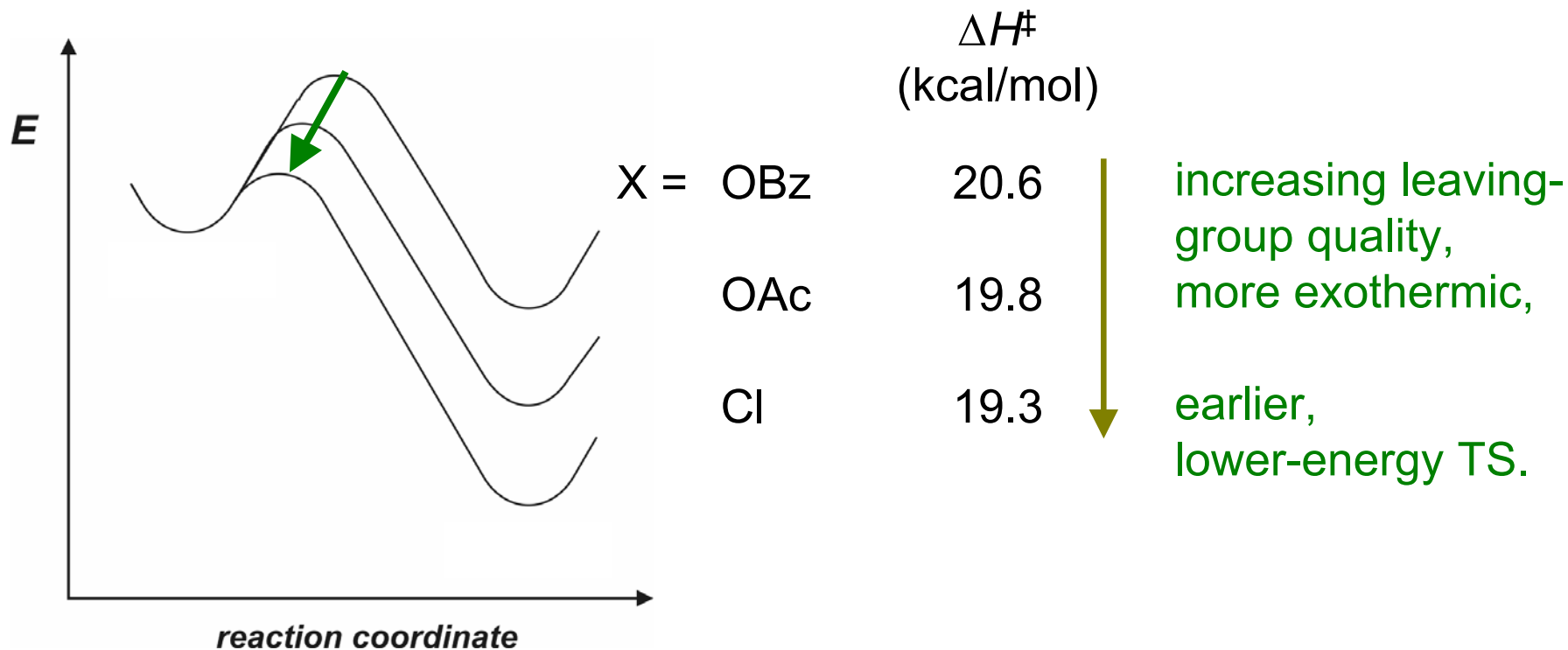


	ΔH^\ddagger (kcal/mol)
B = KOtBu	18.8
NaOEt	19.3
NaOPh	20.2

decreasing basicity,
decreasing $[\text{BH}]/[\text{B}^-]$,
less exothermic,

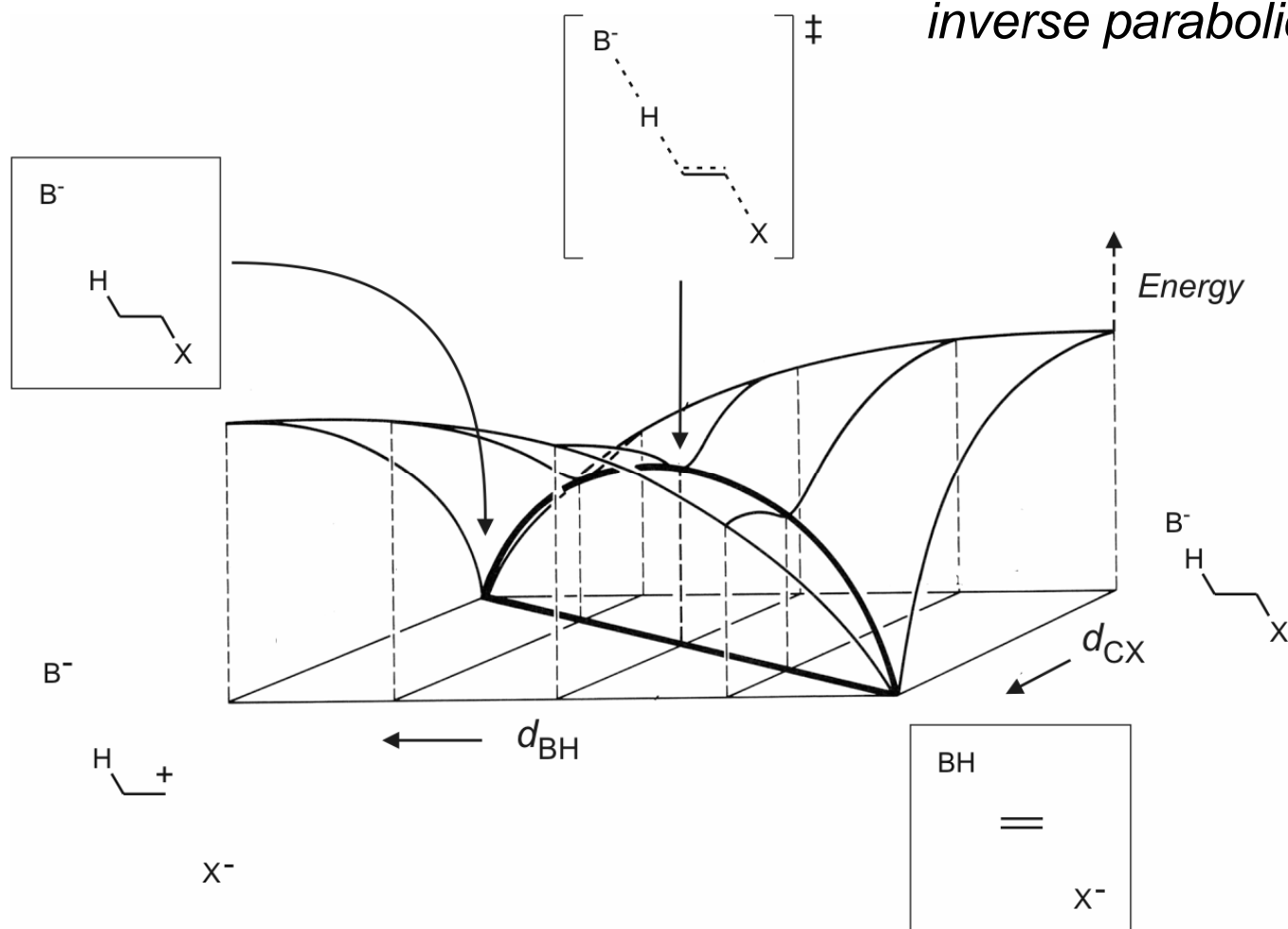
later,
higher-energy TS.

Hammond Postulate Example: E2 Elimination



O'Ferrall Plots: Visualizing Hammond

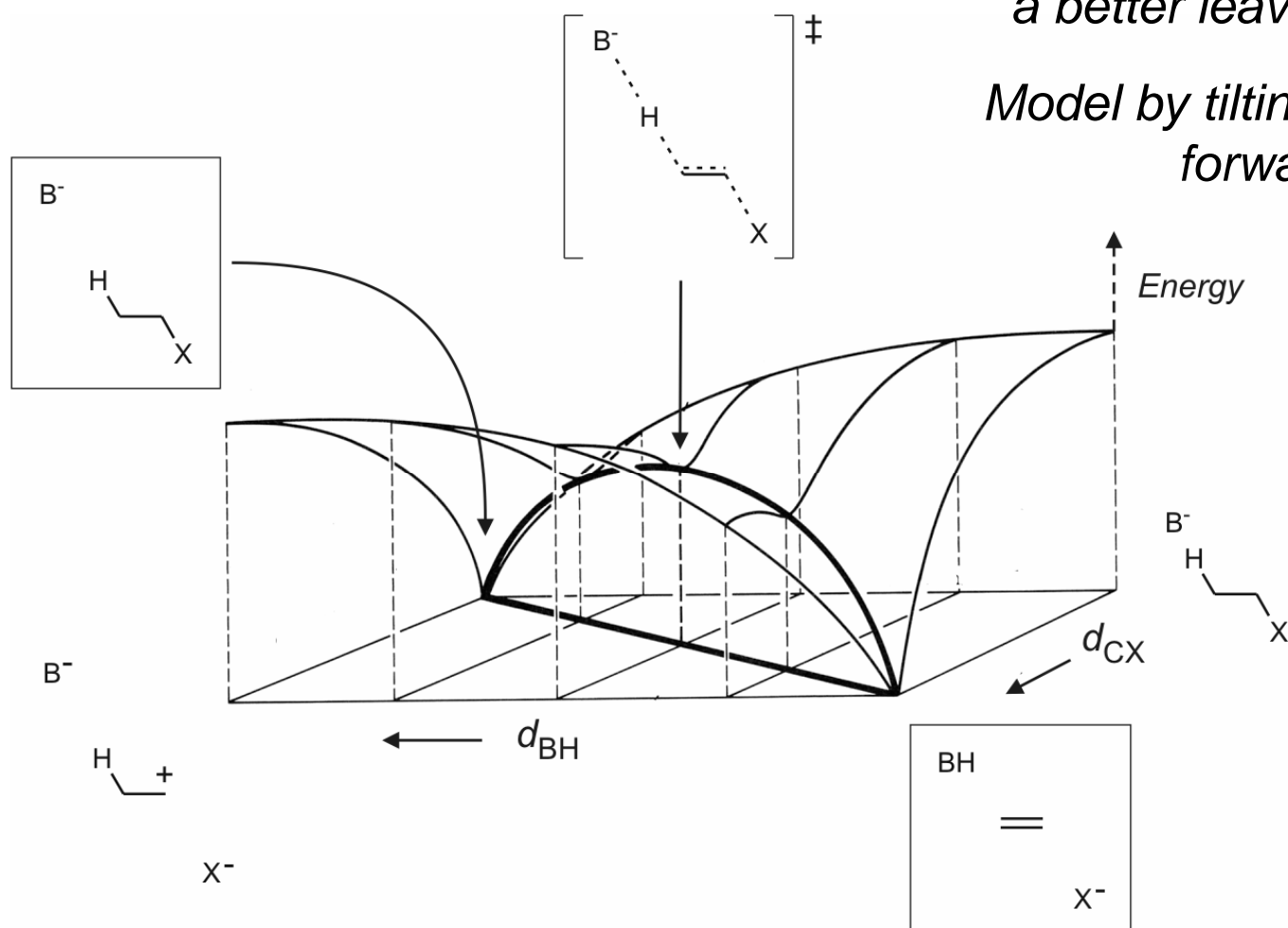
Can model reaction coordinate as inverse parabolic potential well.



O'Ferrall Plots: Visualizing Hammond

*What happens when we make X
a better leaving group?*

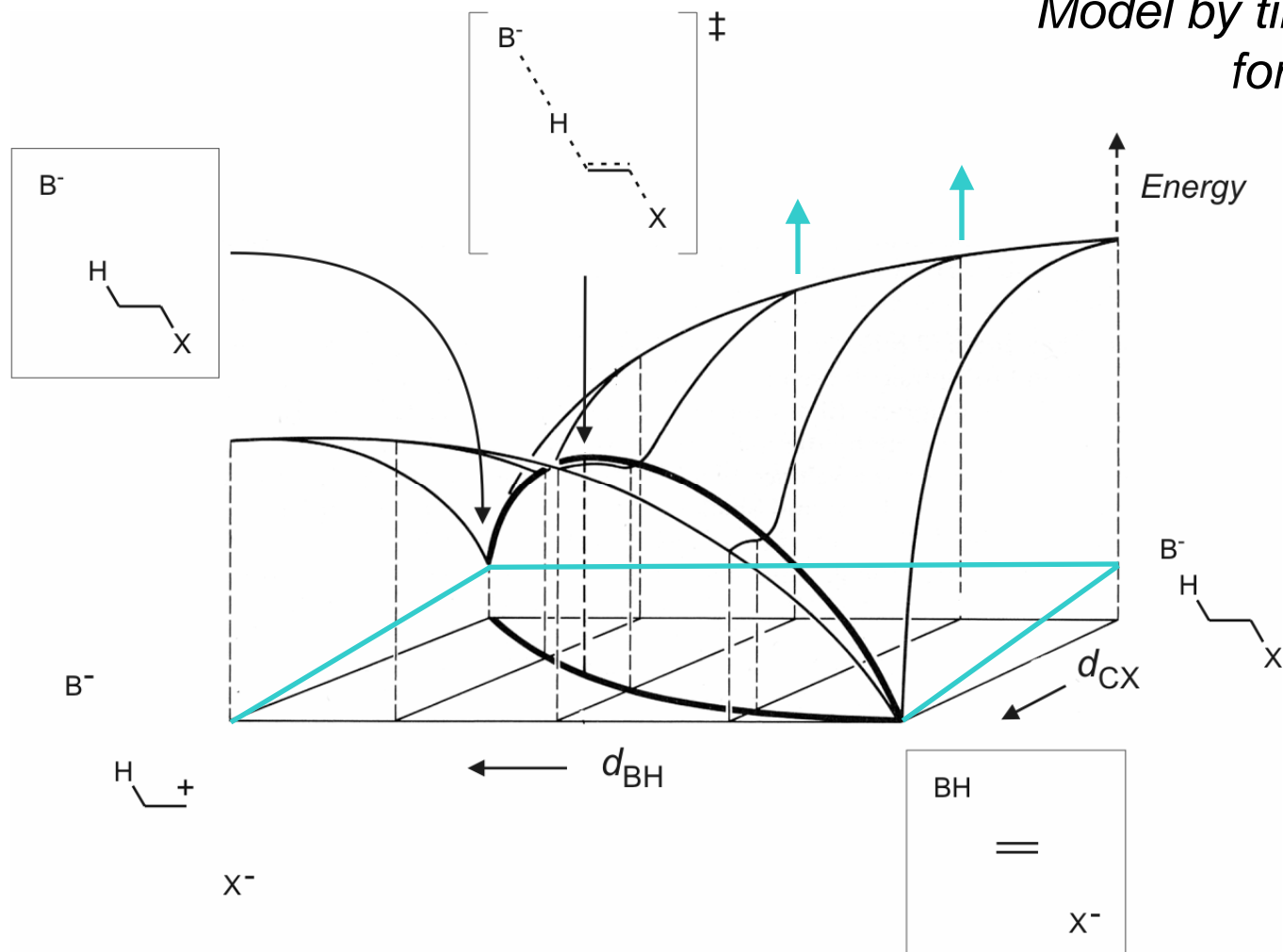
*Model by tilting entire plot
forward.*



O'Ferrall Plots: Visualizing Hammond

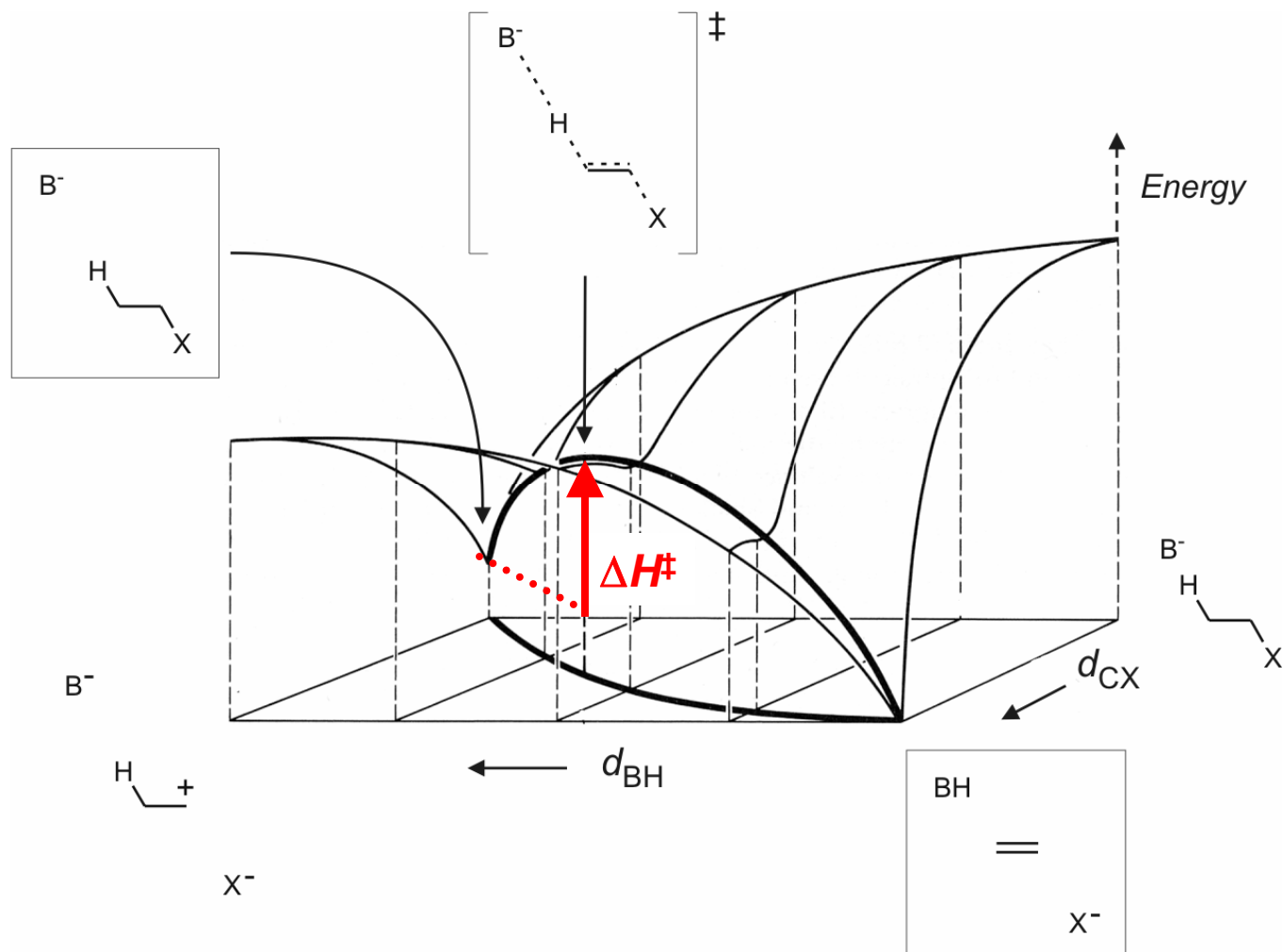
What happens when we make X a better leaving group?

Model by tilting entire plot forward.



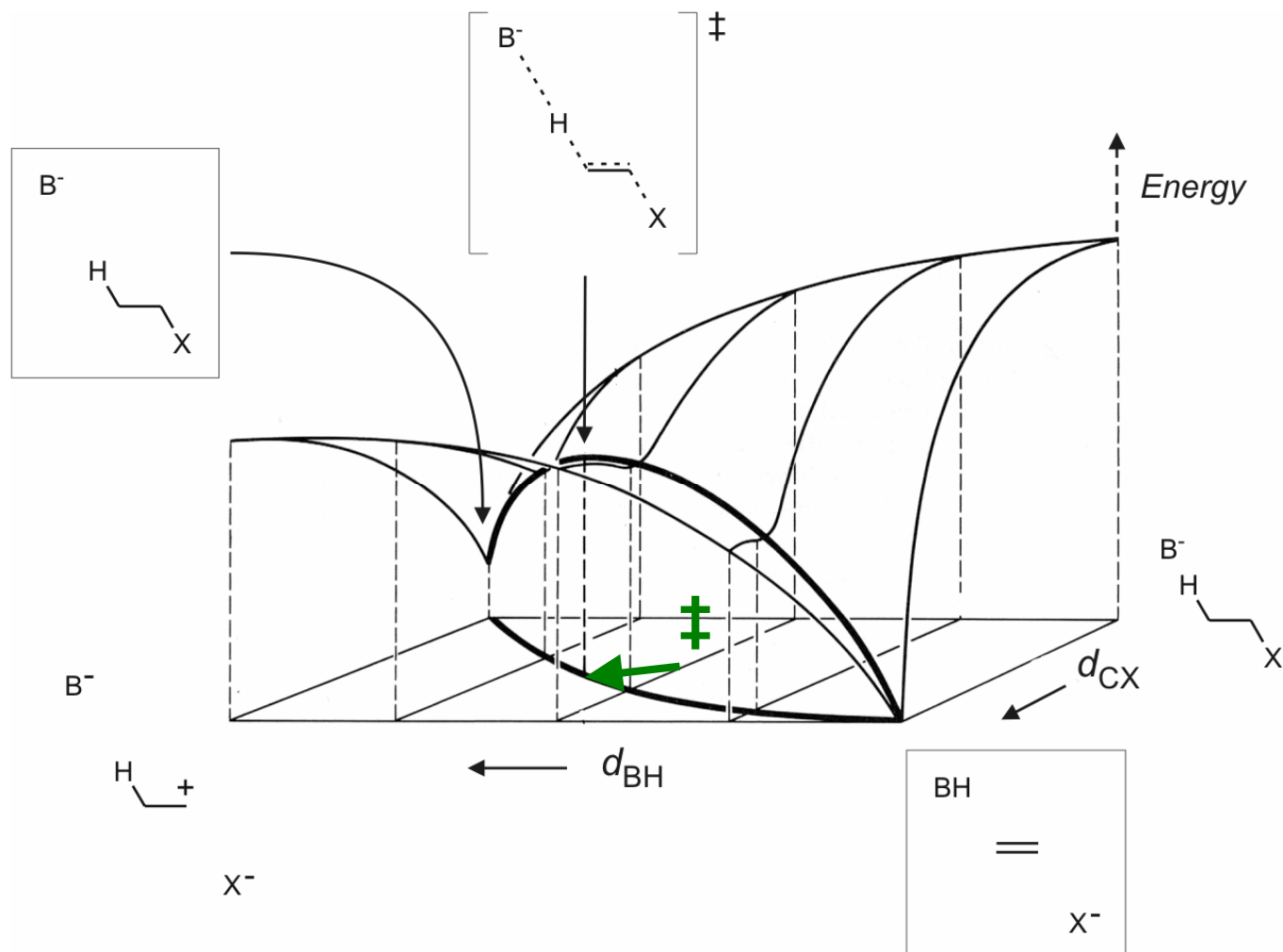
O'Ferrall Plots: Visualizing Hammond

Result: ΔH^\ddagger decreases (as reaction becomes more exothermic)



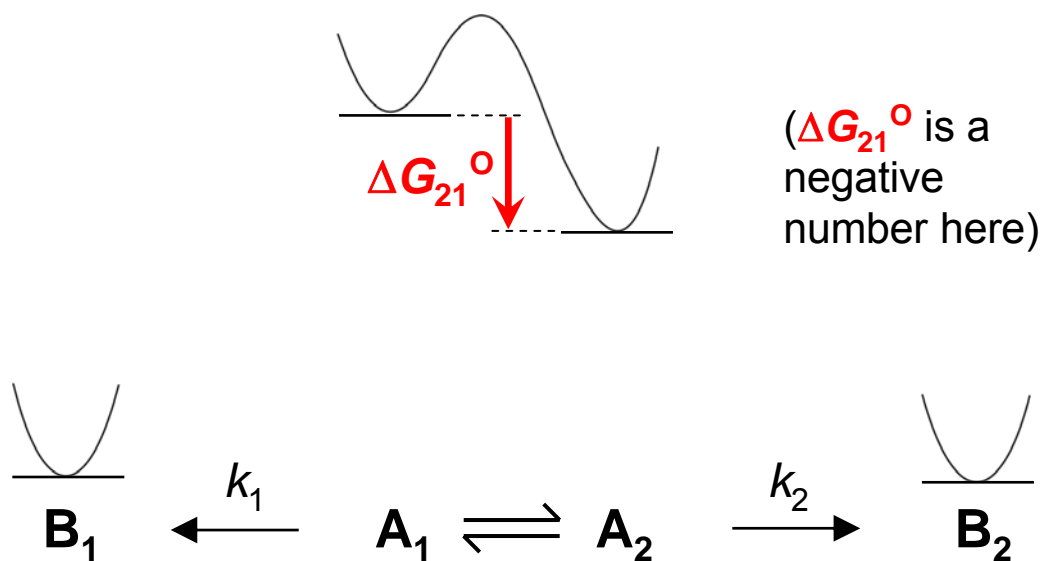
O'Ferrall Plots: Visualizing Hammond

Result: Transition state occurs "earlier", looks more like starting materials.



The Curtin-Hammett Principle

Question: Given an equilibrium that favors starting material A_2 over A_1 , which product is favored: B_1 or B_2 ?



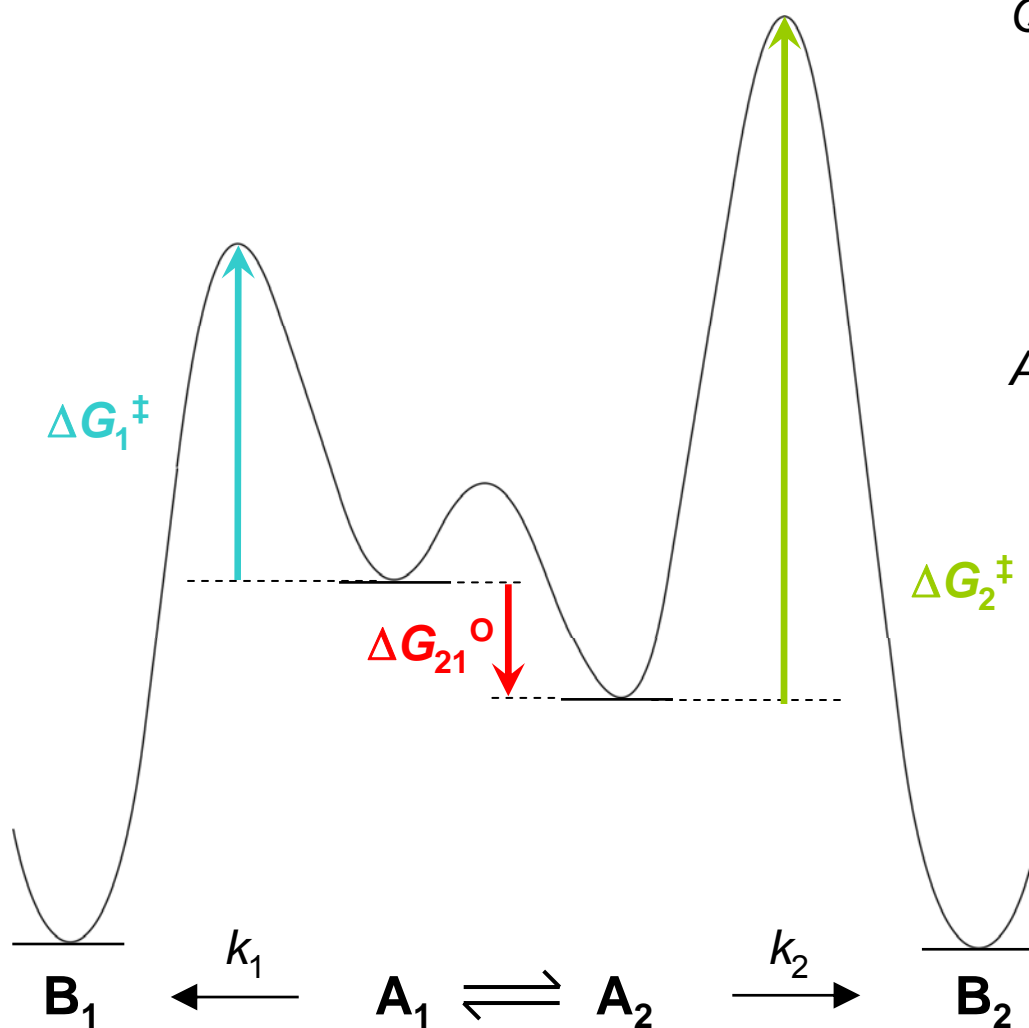
i.e., if

$$K_{\text{eq}} = \frac{[A_2]}{[A_1]} = e^{\left(\frac{-\Delta G_{21}^\circ}{RT}\right)}$$

then what is

$$\frac{\text{rate}_2}{\text{rate}_1} = \frac{\frac{\partial[B_2]}{\partial t}}{\frac{\partial[B_1]}{\partial t}} \quad ?$$

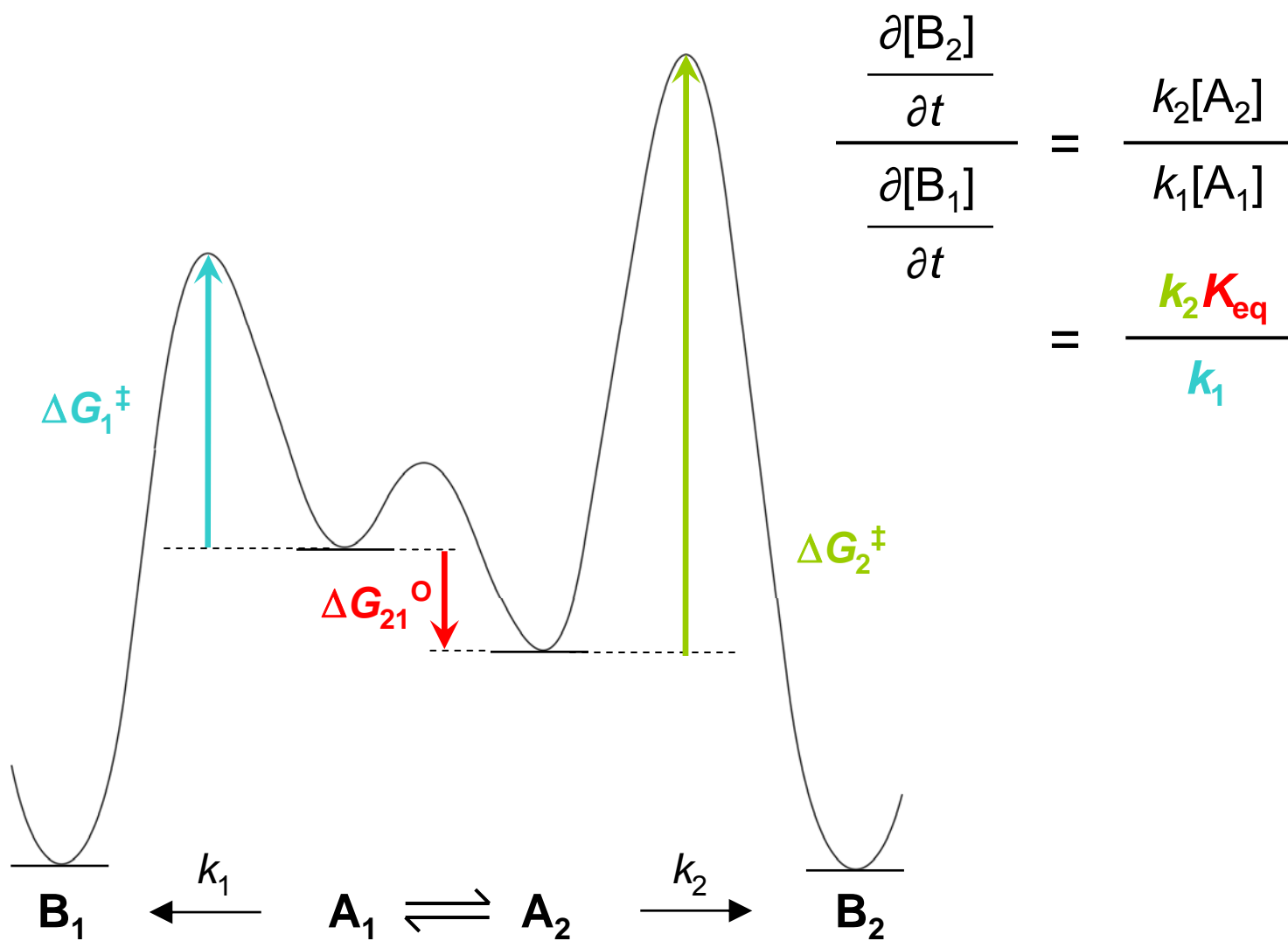
The Curtin-Hammett Principle



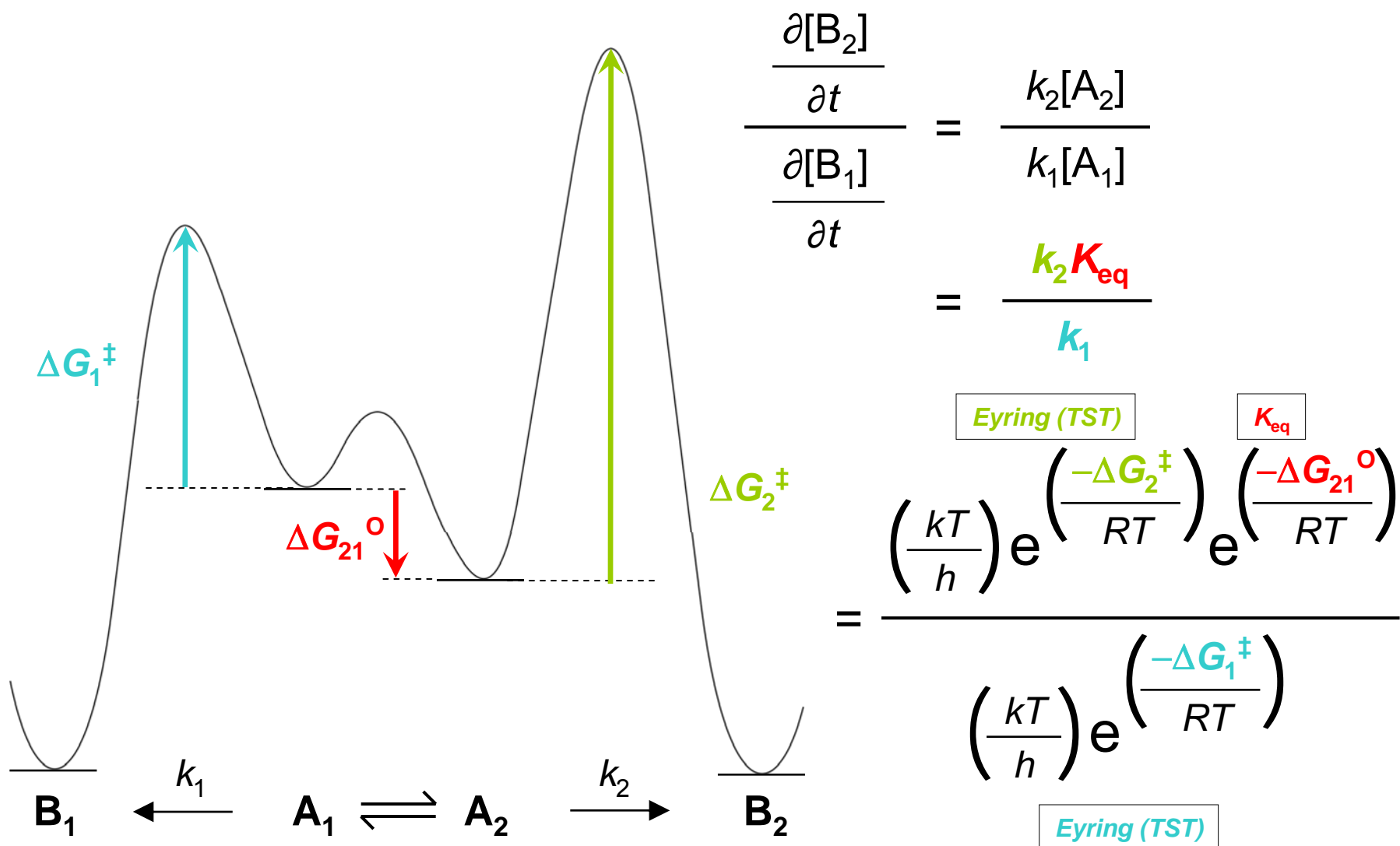
Question: Given an equilibrium that favors starting material A_2 over A_1 , which product is favored: B_1 or B_2 ?

Answer: Depends solely on relative transition state energies, **not** on equilibrium.

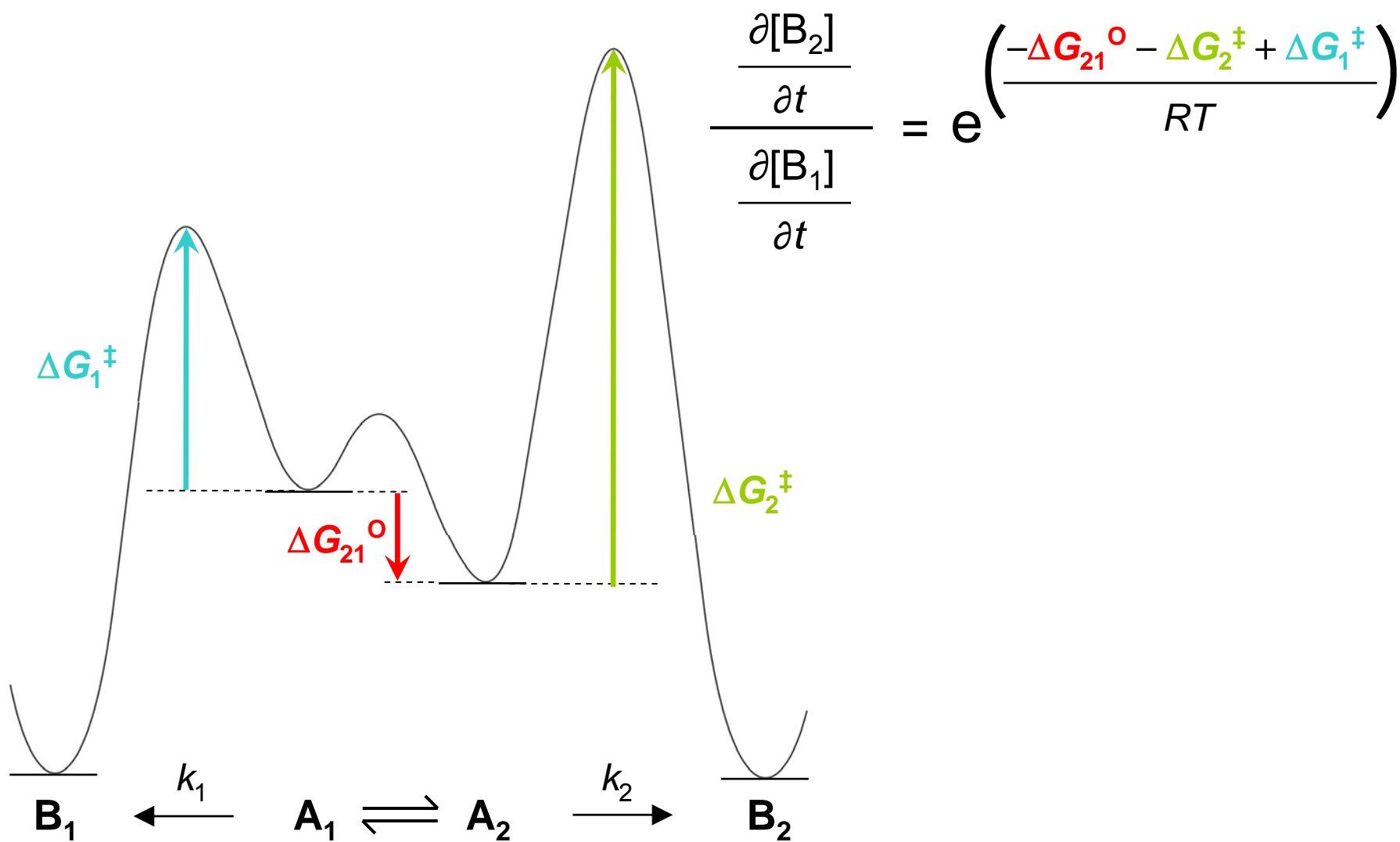
The Curtin-Hammett Principle



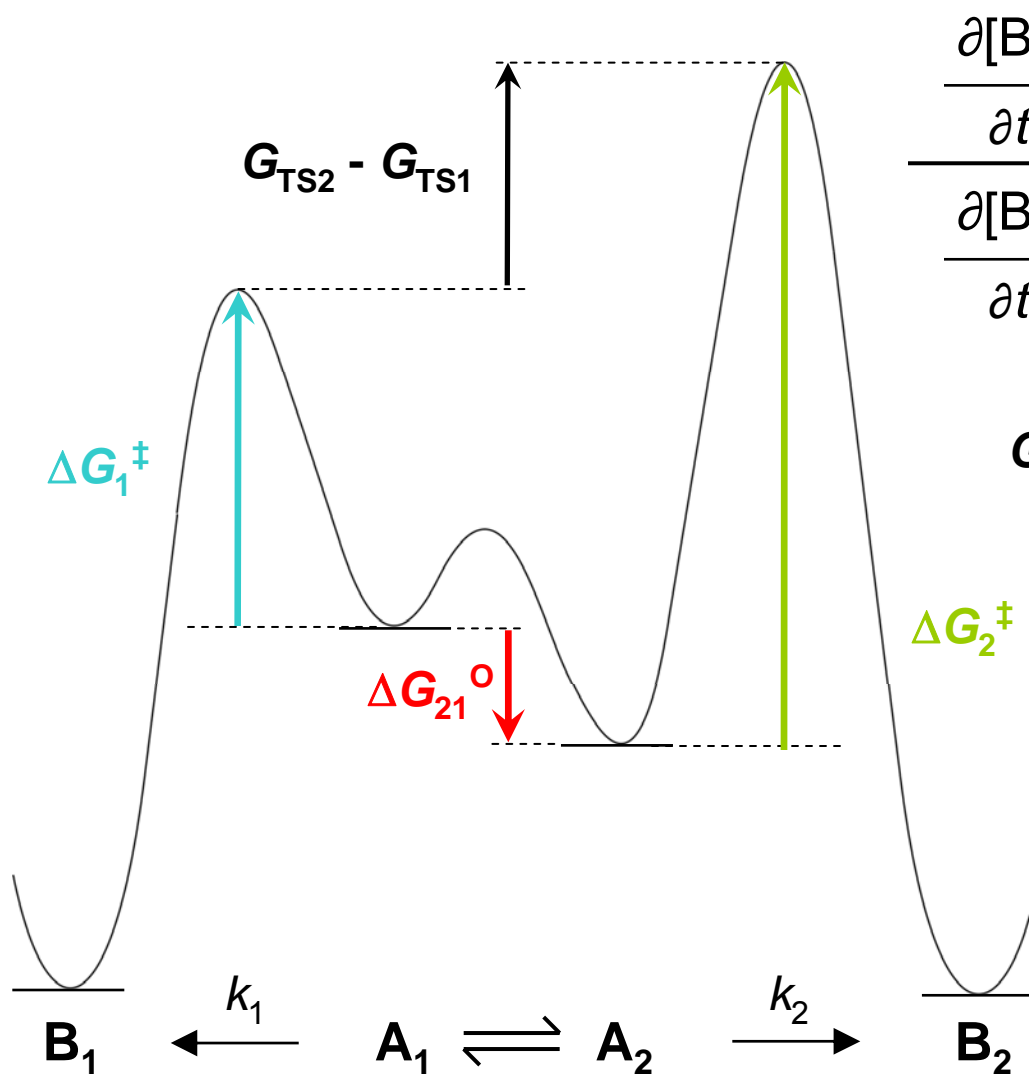
The Curtin-Hammett Principle



The Curtin-Hammett Principle



The Curtin-Hammett Principle



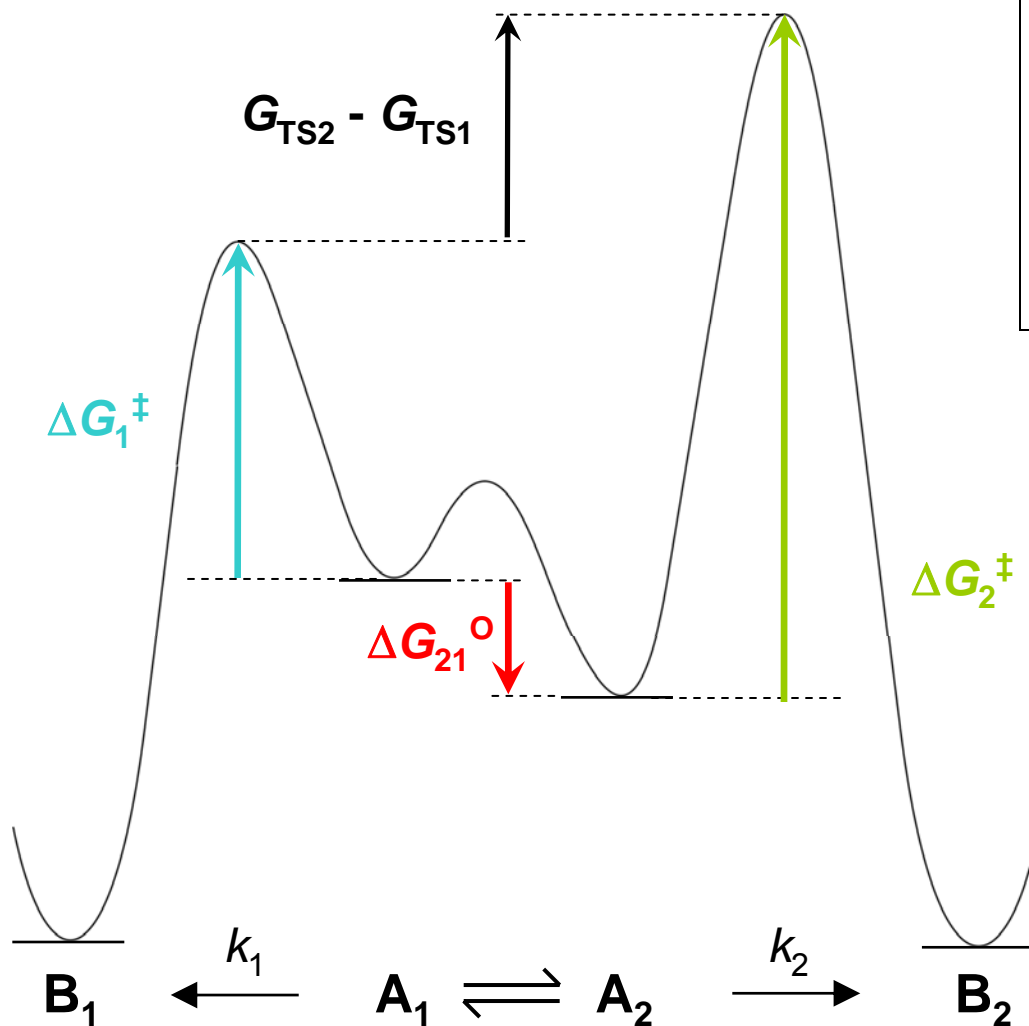
$$\frac{\frac{\partial[B_2]}{\partial t}}{\frac{\partial[B_1]}{\partial t}} = e^{\left(\frac{-\Delta G_{21}^\circ - \Delta G_2^\ddagger + \Delta G_1^\ddagger}{RT} \right)}$$

$$G_{TS2} - G_{TS1} = \Delta G_2^\ddagger - \Delta G_1^\ddagger + \Delta G_{21}^\circ$$

↑
(because ΔG_{21}°
written as negative
number)

$$\frac{\frac{\partial[B_2]}{\partial t}}{\frac{\partial[B_1]}{\partial t}} = e^{\left(\frac{-(G_{TS2} - G_{TS1})}{RT} \right)}$$

The Curtin-Hammett Principle



$$\frac{\frac{\partial[B_2]}{\partial t}}{\frac{\partial[B_1]}{\partial t}} = e^{\left(\frac{-(G_{TS2} - G_{TS1})}{RT}\right)}$$

So, relative reaction rates depend only on relative transition-state energies, and not on starting-material ground-state energies.