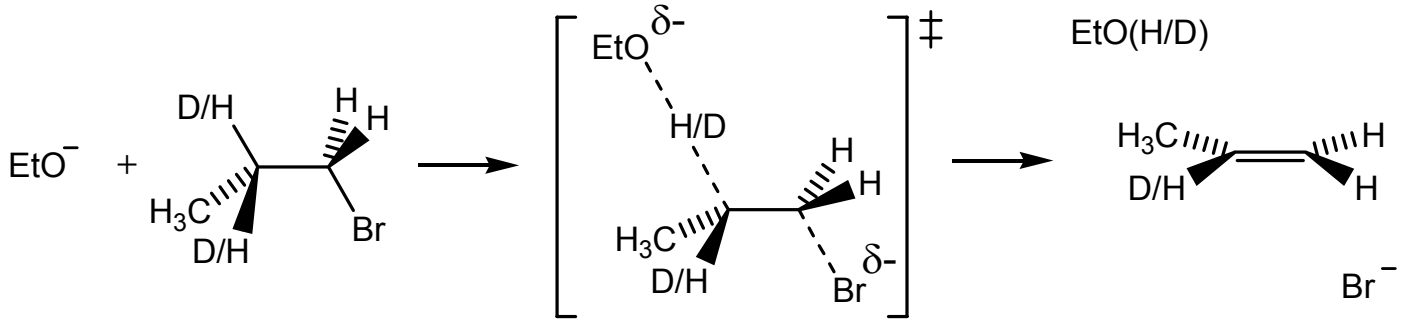
# Kinetic Isotope Effects

Isotope effects more interesting when they tell us about character of rate-determining transition state.

Example:



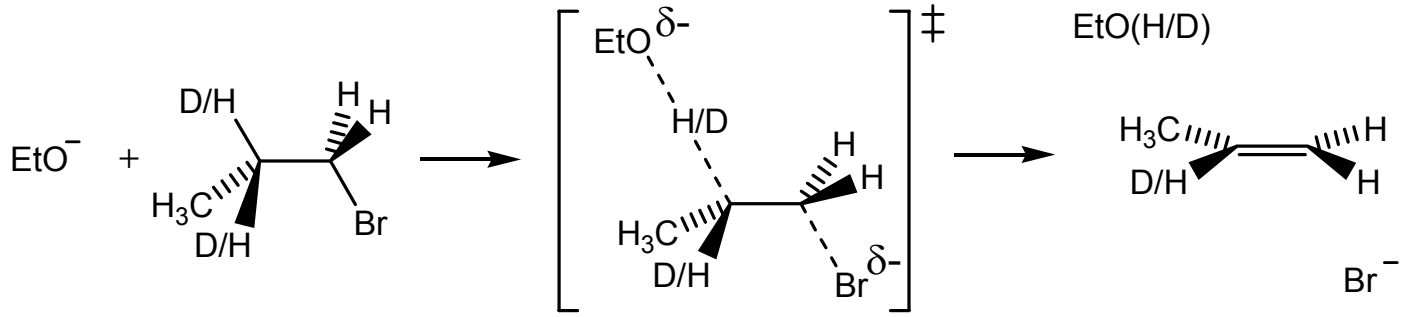

How should isotopic substitution affect rate in this reaction?

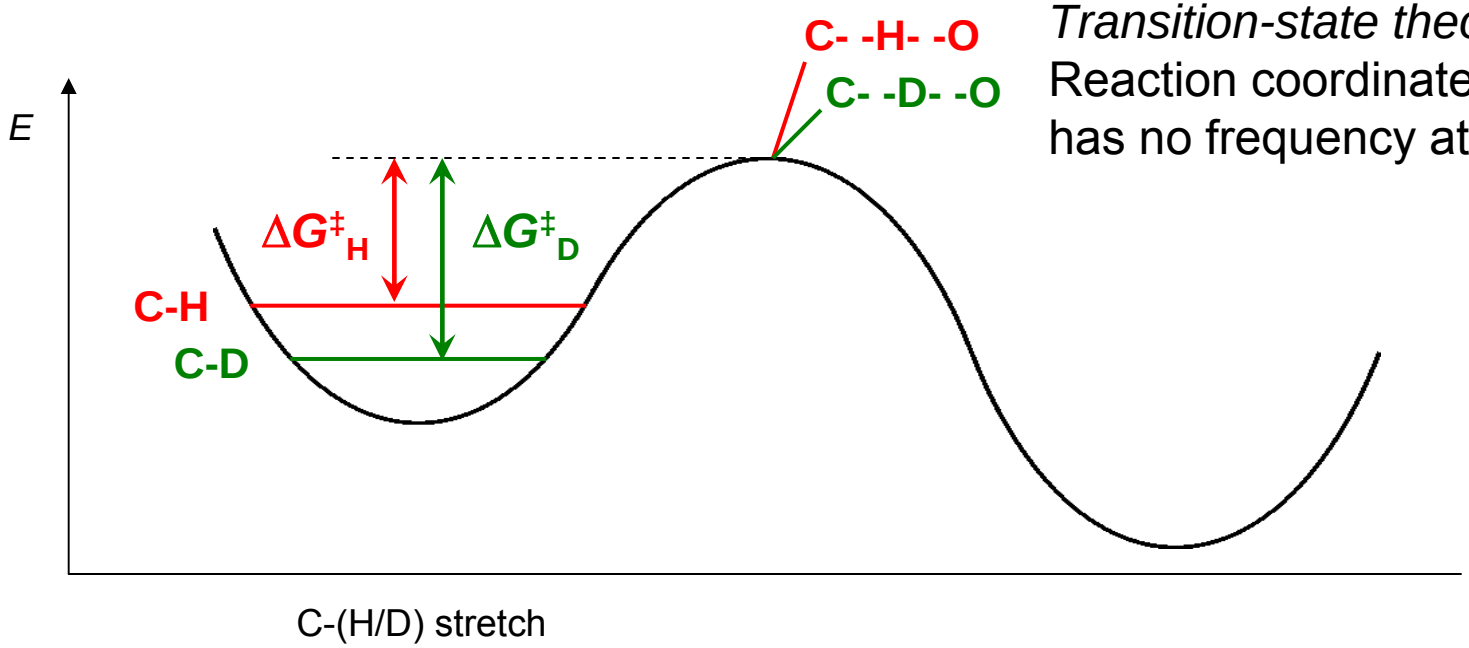
*or*

How does isotopic substitution affect relative energies of starting material and transition state?

# Primary Kinetic Isotope Effects

1° KIE: Isotope participates directly in reaction.

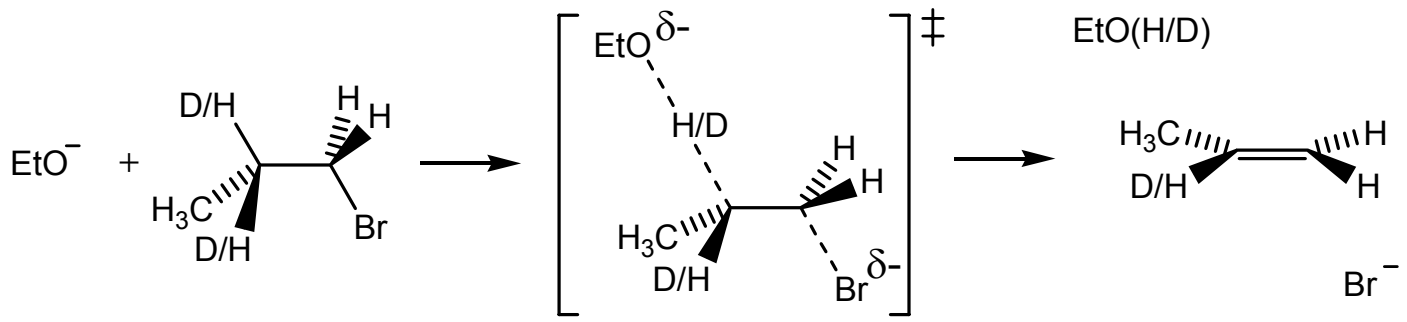


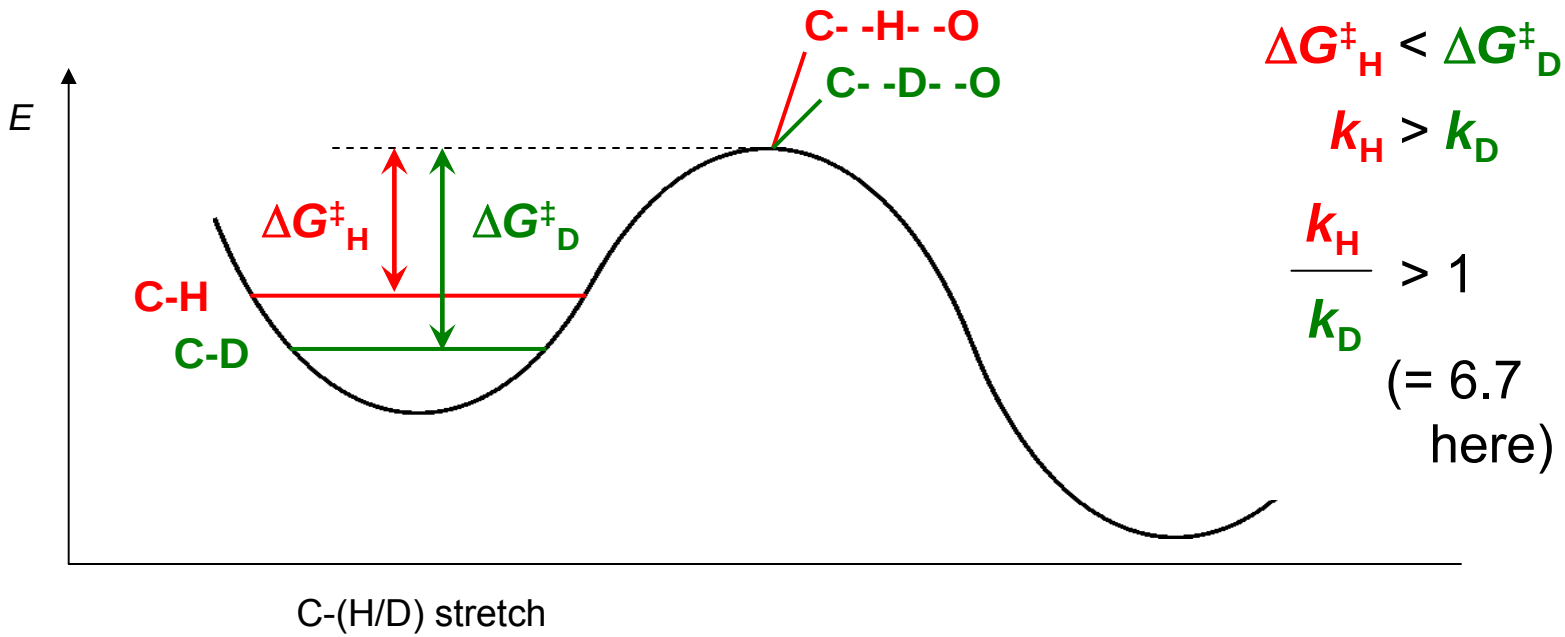




*Transition-state theory says:*
Reaction coordinate mode has no frequency at TS.

# Primary Kinetic Isotope Effects

1° KIE: Isotope participates directly in reaction.

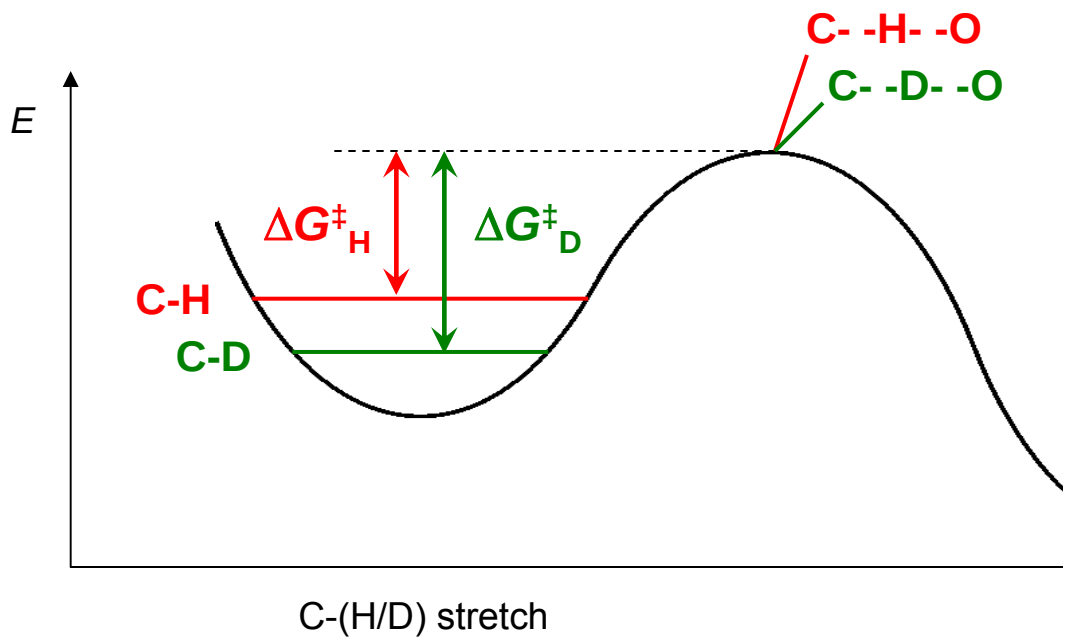



$\Delta G^{\ddagger}_{H} < \Delta G^{\ddagger}_{D}$

$k_H > k_D$

$\frac{k_H}{k_D} > 1$ (= 6.7 here)



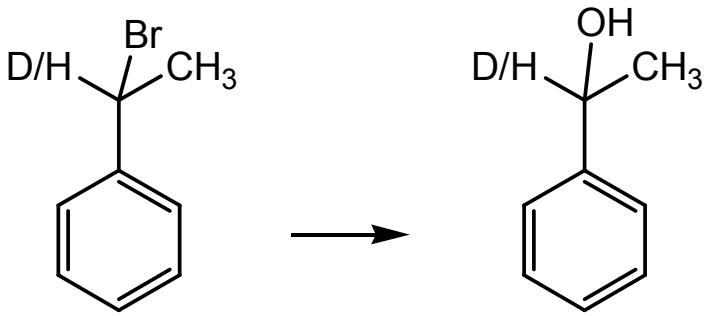

$$\frac{k_H}{k_D} = \frac{\frac{k_B T}{h} e^{\frac{-\Delta G_H^{\ddagger}}{RT}}}{\frac{k_B T}{h} e^{\frac{-\Delta G_D^{\ddagger}}{RT}}}$$

$$= e^{\frac{\Delta G_D^{\ddagger} - \Delta G_H^{\ddagger}}{RT}}$$

$$= e^{\frac{\mathrm{ZPE(C–H)} - \mathrm{ZPE(C–D)}}{RT}}$$

# Secondary Kinetic Isotope Effects

Isotope effects still observed when isotope is not directly involved in reaction coordinate. (Called 2° KIE.)

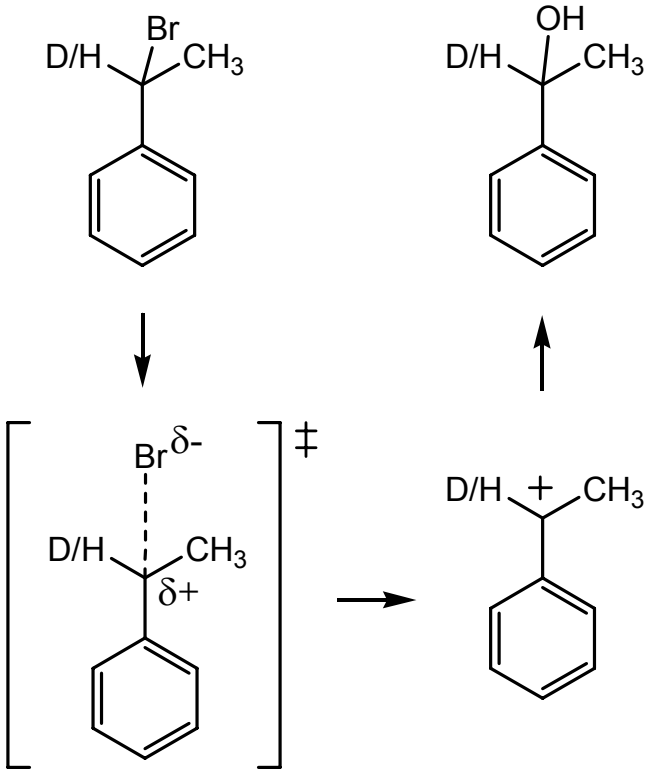



$$\frac{k_H}{k_D} = 1.1$$

*(seems small, but very reproducible)*

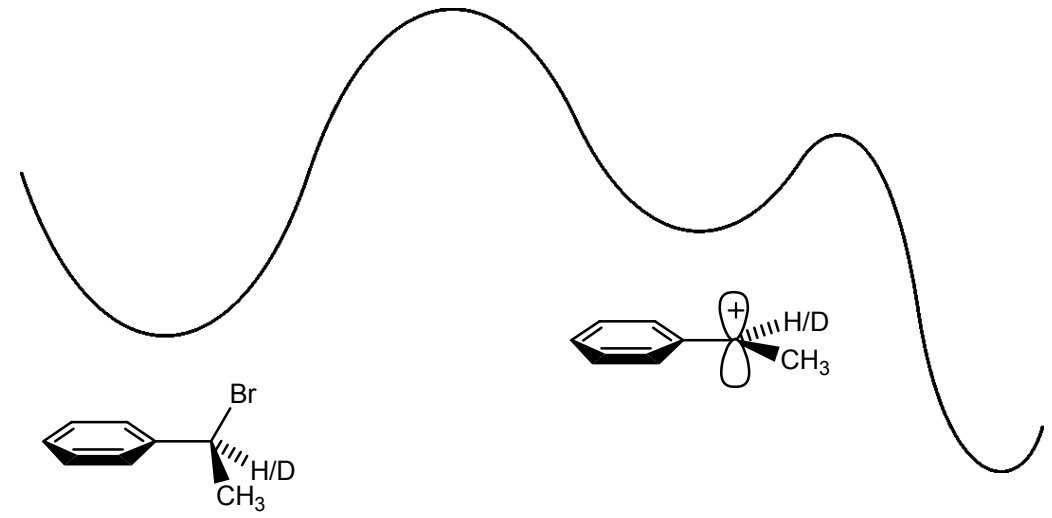
Here, C-(H/D) bond is not part of reaction coordinate.

# Secondary Kinetic Isotope Effects




Before, we asked how vibrational modes changed over course of reaction.

How about now?




(C-Br bond breaking)

(C-O bond making)

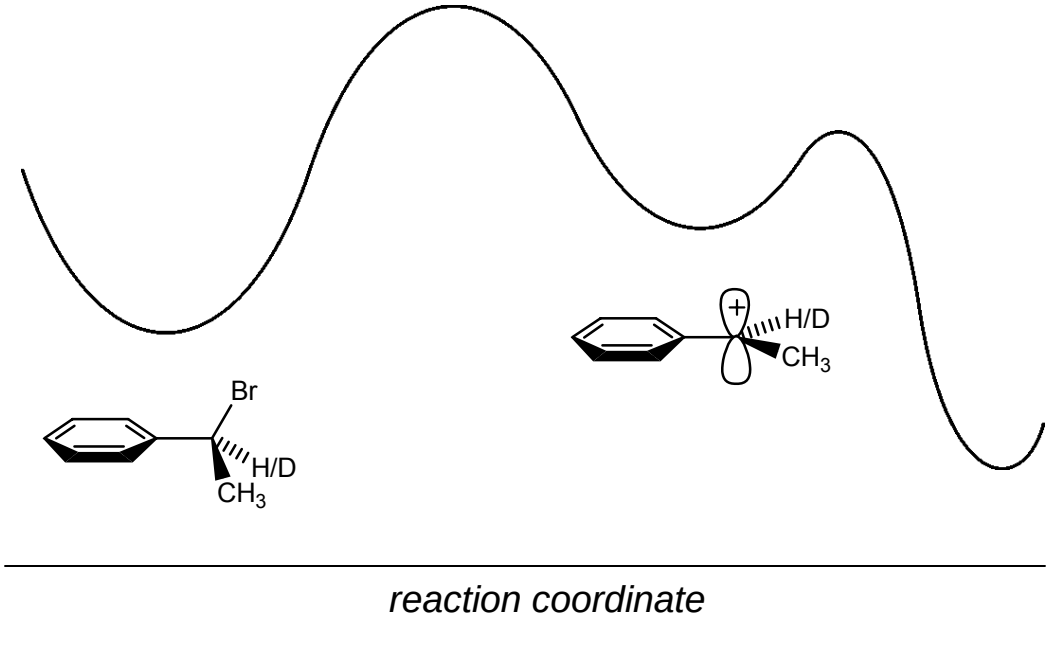
# Secondary Kinetic Isotope Effects

| | *starting material* $C_{sp^3}$-H | *intermediate* $C_{sp^2}$-H |
|---|---|---|
| $\nu_{stretch}$ = | 2950 $cm^{-1}$ | 3050 $cm^{-1}$ |
| $\nu_{in\text{-}plane\ wag}$ = | 1350 $cm^{-1}$ | 1350 $cm^{-1}$ |
| $\nu_{out\text{-}of\text{-}plane\ wag}$ = | 1350 $cm^{-1}$ | 800 $cm^{-1}$ |

**Largest $\Delta\nu$. We'll consider this mode.**

Before, we asked how vibrational modes changed over course of reaction.

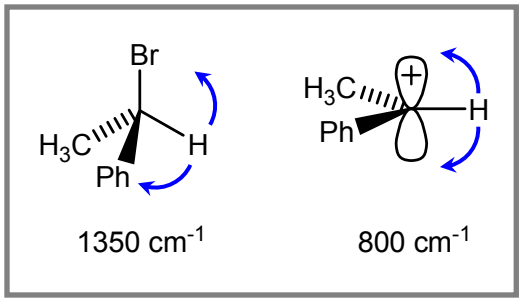
How about now?

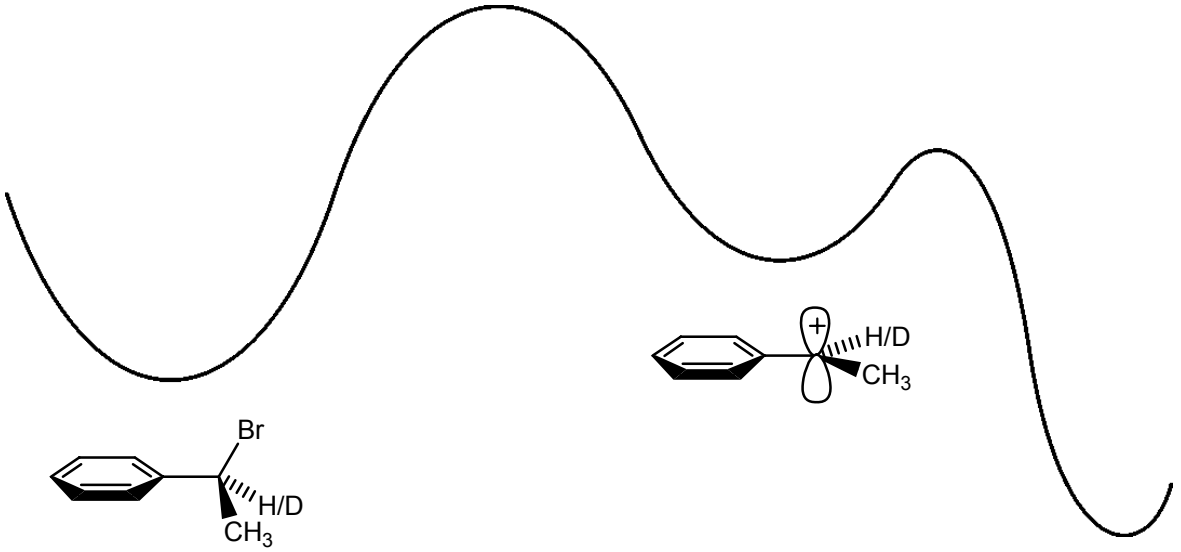



(C-Br bond breaking)

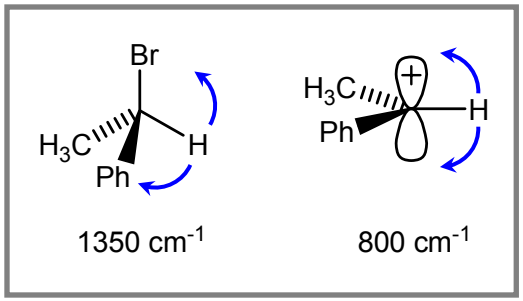
(C-O bond making)

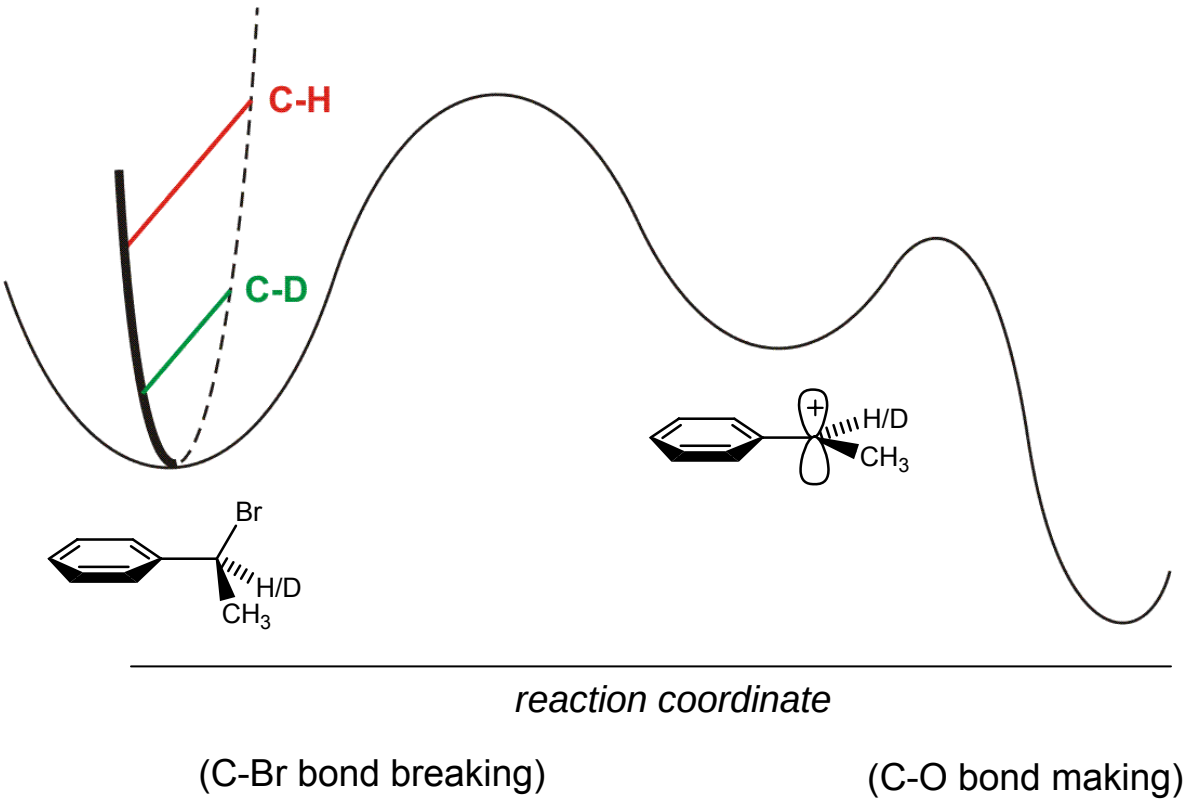
# Secondary Kinetic Isotope Effects



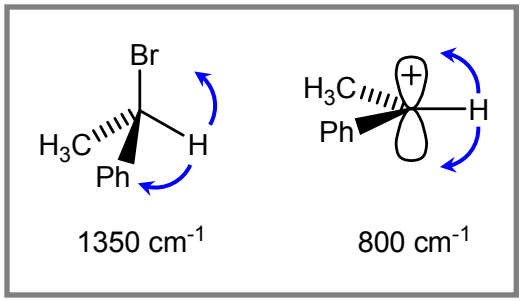



# Secondary Kinetic Isotope Effects

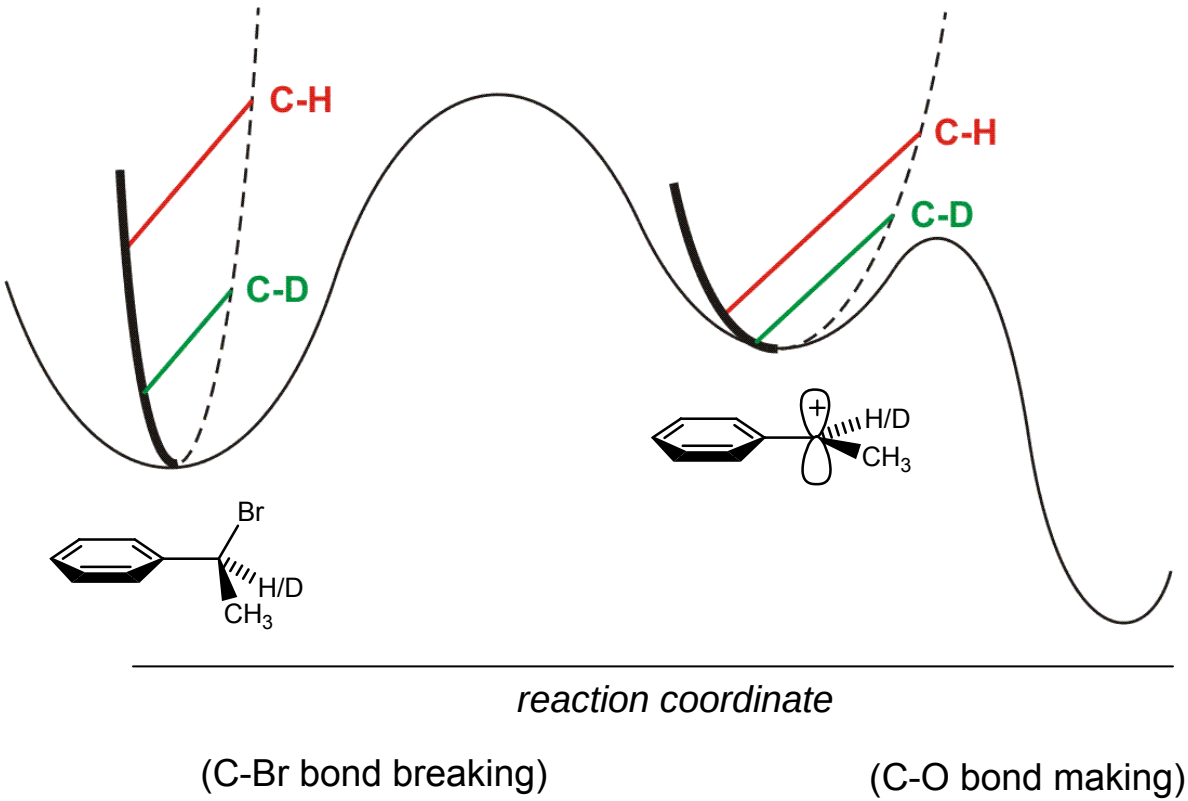


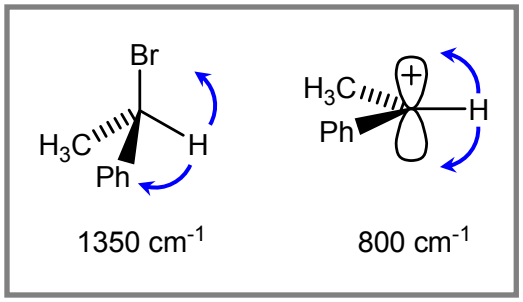
# Secondary Kinetic Isotope Effects




*We don't know what transition-state frequency is; assume is between starting material and product.*



# Secondary Kinetic Isotope Effects

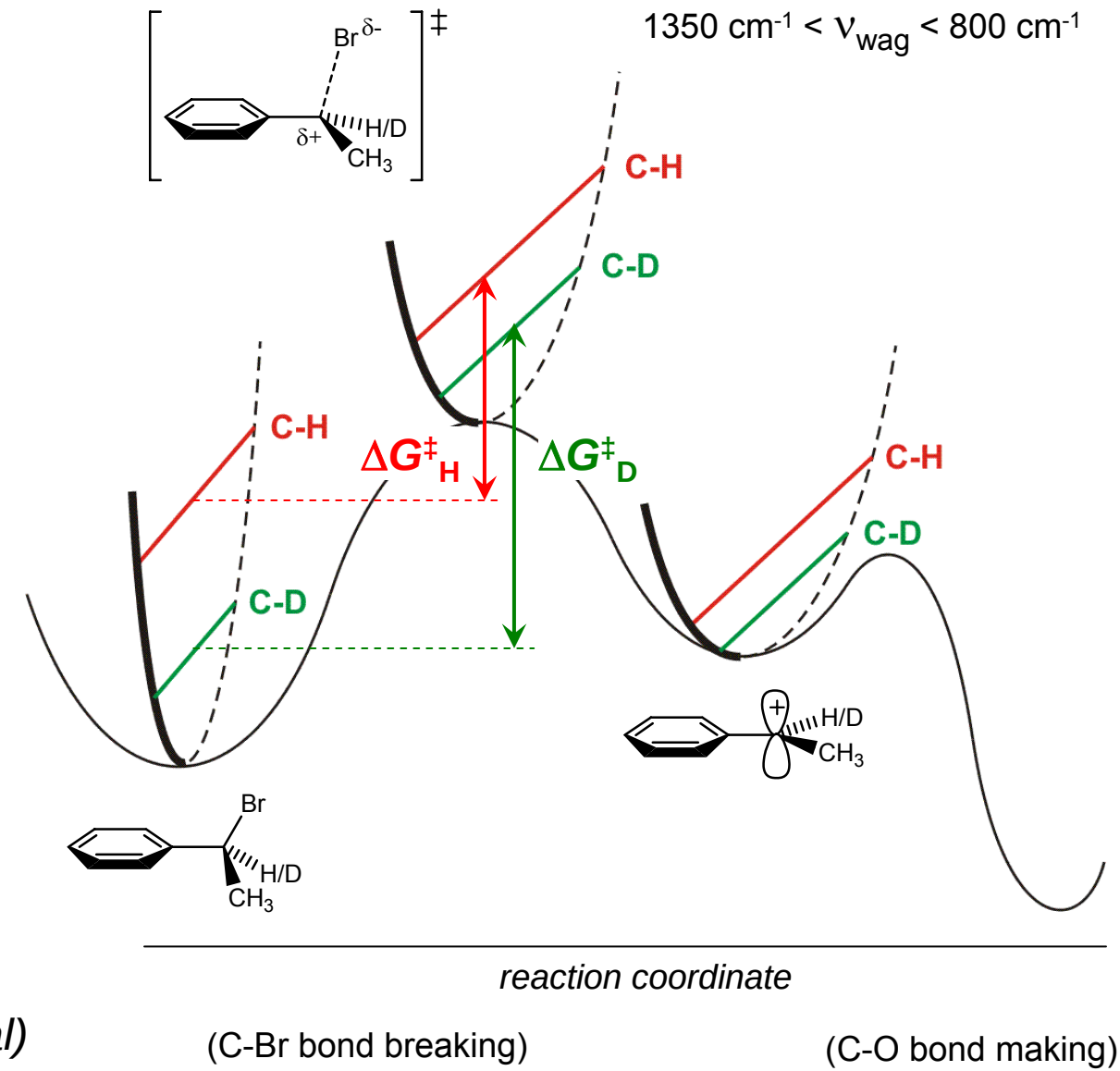



$\Delta G^{\ddagger}_{H} < \Delta G^{\ddagger}_{D}$

$k_H > k_D$

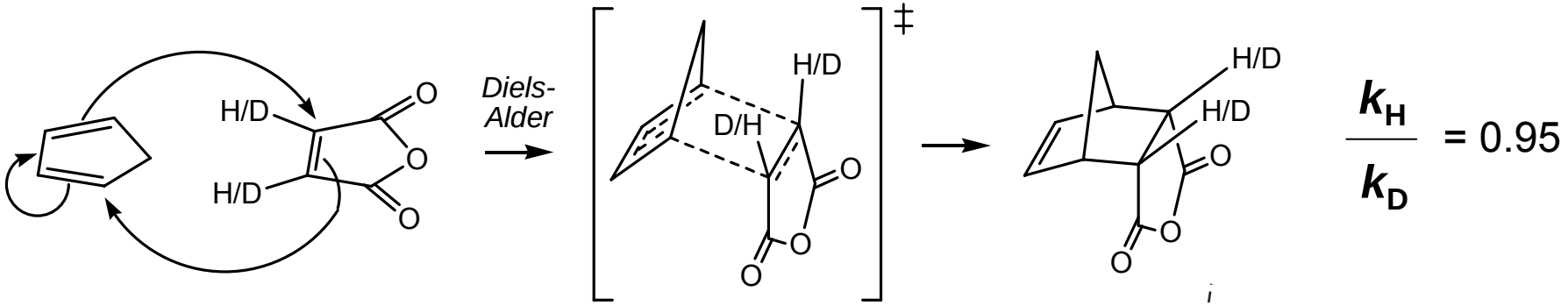
$\frac{k_H}{k_D} > 1$ (= 1.1 here)

*> 1 because ν decreased in rate-determining step (relative to starting material)*



# Secondary Kinetic Isotope Effects

$\frac{k_H}{k_D}$ can also be < 1:




$sp^2 \rightarrow sp^3$ hybridization at C-H/D shows opposite trend from previous example;

$$\Delta G^{\ddagger}_H > \Delta G^{\ddagger}_D$$

$$k_H < k_D$$

$$\frac{k_H}{k_D} < 1$$