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

$1^\circ$ KIE: Isotope participates directly in reaction.

Transition-state theory says: Reaction coordinate mode has no frequency at TS.
Primary Kinetic Isotope Effects

$1^\circ$ KIE: Isotope participates directly in reaction.

\[
\text{EtO}^- + \text{H}_3\text{C} \rightarrow \text{EtO}^\delta+ \rightarrow \text{H}_3\text{C} \rightarrow \text{EtO}(\text{H/D})
\]

\[
\Delta G^\ddagger_\text{H} < \Delta G^\ddagger_\text{D} \quad \frac{k_\text{H}}{k_\text{D}} > 1 \quad (= 6.7 \text{ here})
\]
\[ \frac{k_H}{k_D} = \frac{k_B T}{h} e^{\frac{-\Delta G_D^\ddagger}{RT}} \]

\[ \frac{\Delta G_D^\ddagger - \Delta G_H^\ddagger}{RT} = e^{\frac{ZPE(C-H) - ZPE(C-D)}{RT}} \]
Secondary Kinetic Isotope Effects

Isotope effects still observed when isotope is not directly involved in reaction coordinate. (Called $2^\circ$ KIE.)

\[
\frac{k_H}{k_D} = 1.1 \quad \text{(seems small, but very reproducible)}
\]

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?
Primary Kinetic Isotope Effects

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How about now?

\[ \nu_{\text{stretch}} = 2950 \text{ cm}^{-1} \quad 3050 \text{ cm}^{-1} \]

\[ \nu_{\text{in-plane wag}} = 1350 \text{ cm}^{-1} \quad 1350 \text{ cm}^{-1} \]

\[ \nu_{\text{out-of-plane wag}} = 1350 \text{ cm}^{-1} \quad 800 \text{ cm}^{-1} \]

Largest \( \Delta \nu \). We’ll consider this mode.
Secondary Kinetic Isotope Effects

![Diagram showing reaction coordinate and bond breaking/making](image)

1350 cm\(^{-1}\)  800 cm\(^{-1}\)

(C-Br bond breaking)  (C-O bond making)
Secondary Kinetic Isotope Effects

(C-Br bond breaking)  (C-O bond making)
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 \( \nu \) decreased in rate-determining step (relative to starting material)

1350 cm\(^{-1}\) < \( \nu_{\text{wag}} \) < 800 cm\(^{-1}\)

\( \Delta G^\ddagger_H \) (C-Br bond breaking)
\( \Delta G^\ddagger_D \) (C-O bond making)
Secondary Kinetic Isotope Effects

\[
\frac{k_H}{k_D} \text{ can also be } < 1:
\]

\[
\frac{k_H}{k_D} = 0.95
\]

sp\(^2\) → sp\(^3\) hybridization at C-H/D shows opposite trend from previous example;

\[
\Delta G^{\dagger}_H > \Delta G^{\dagger}_D
\]

\[
k_H < k_D
\]

\[
\frac{k_H}{k_D} < 1
\]