

Kinetic isotope effects

- Kinetic isotope effects: reaction rates change by isotopic substitution
- Most common substitution: D for H

Origin of the kinetic isotope effect: change in *mass* =>

$$\nu = \frac{1}{2\pi} \sqrt{\frac{k}{m}}$$

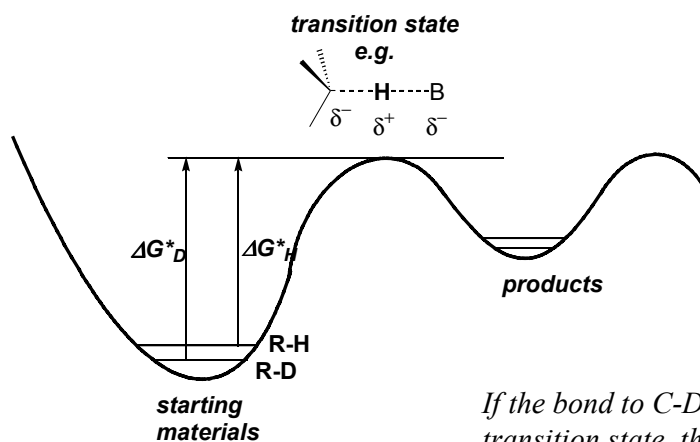
=> change in *vibrational energy levels*

$$E_n = (n + 1/2)h\nu$$

When $n = 0$, we have reached the lowest energy level, which still retains *zero-point energy* ($= 1/2 h\nu$). This energy is proportional to

$$\sqrt{\frac{1}{m}}$$

Kinetic isotope effects: D vs. H

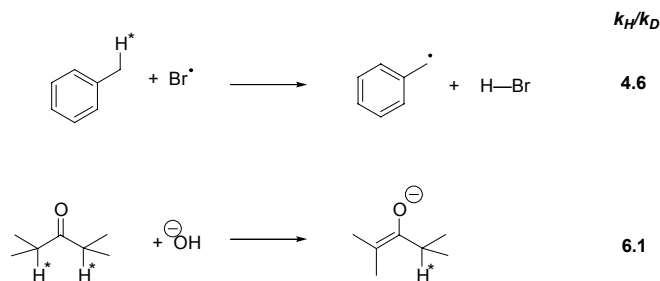


If the bond to C-D is broken in the transition state, the deuterated compound reacts at a slower rate.

It is easier to shake off a lighter atom compared to a heavier one!

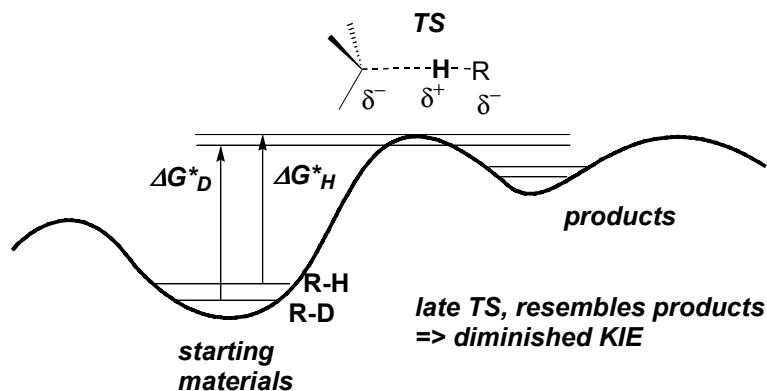
Primary kinetic isotope effects

- C-H bond in IR: 3000 cm^{-1} , C-D: 2200 cm^{-1} $\Rightarrow \Delta E = 1.15\text{ kcal/mol}$
- at 298 K, maximum theoretical kinetic isotope effect (k_H/k_D) = 6.5
- observation of a large kinetic isotope effect gives a very good indication that a bond to C-H is broken in the transition state



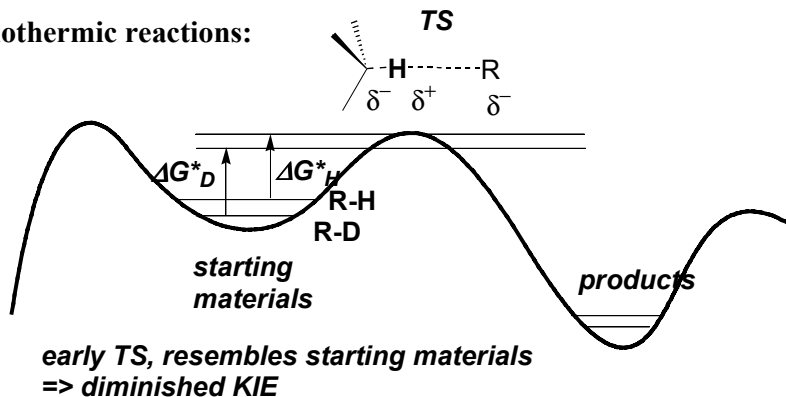
Magnitude of primary kinetic isotope effects

Endothermic reactions:



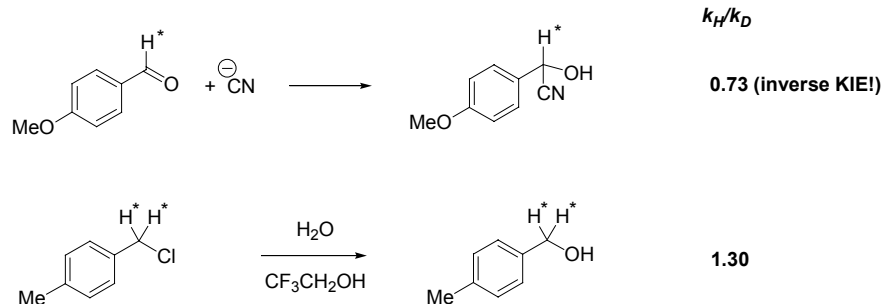
Magnitude of primary kinetic isotope effects 2

Exothermic reactions:

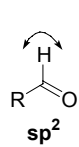


Secondary kinetic isotope effects

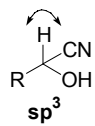
- Secondary KIE: effect of an isotope substituent on a bond *that is not broken in the TS*
- typically close to the reaction center (α , β , γ)
- result from tightening or loosening of the C-H bond in the TS (e.g. because of change in hybridization):



Inverse or normal secondary KIE?

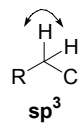


resistance
to bending
increases

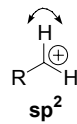


Heavier atoms are less
affected if bending becomes
more difficult

=> inverse KIE



resistance
to bending
decreases



Lighter atoms gain more
if bending becomes easier

=> normal KIE
