

Determining and Describing Chemical Mechanisms, Continued, to recapitulate

1. **Cross-over experiments**
2. **Isotopic Labeling**
3. **Determination of ΔH^\ddagger and ΔS^\ddagger .**
4. **Synthesize the intermediate under the reaction conditions**
5. **Calculations**
6. **Synthesis of intermediates**
7. **Stereochemical labels**
8. **Solvent effects**
9. **Molecularity**
10. **Kinetic Isotope Effects (KIE)**

10.1. **Primary Kinetic Isotope Effect (PKIE)**

10.2. Reactions occur along vibrational modes

10.2.1. When heavy atoms are attached bonds vibrate slower—less energetically.

$$10.2.2. \bar{\nu} = \frac{1}{2\pi c} \sqrt{\frac{f}{M_x M_y / (M_x + M_y)}}$$

10.2.2.1. The equation above more or less determines the wave number (frequency, energy) of a particular vibrational mode.

10.2.3. There is an inverse dependence on the reduced mass, $M_x M_y / (M_x + M_y)$.

10.2.4. One can see that in going from H to D the biggest changes are had in reduced mass.

10.2.4.1. For H-H the reduced mass is $\frac{1}{2}$ amu.

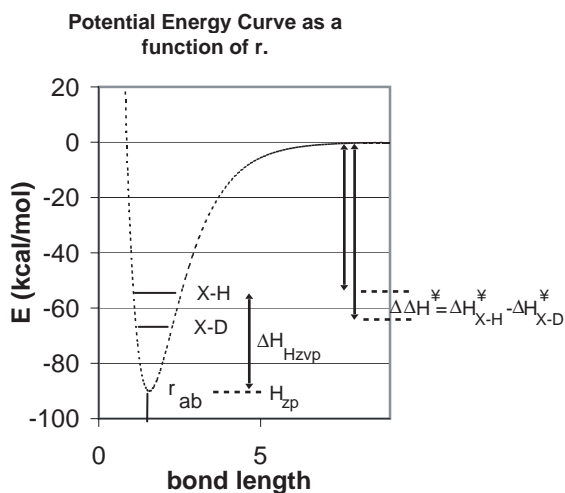
10.2.4.2. For H-D the reduced mass is $\frac{2}{3}$ amu.

10.2.4.2.1. For vibrations involving heavier atoms isotopic changes are less pronounced due to the relative magnitude of the numerator and the denominator in the ratio.

10.2.5. Primary Kinetic Isotope Effect: When reaction rates are compared due to isotopic changes at the reaction center.

10.2.6. Secondary Kinetic Isotope Effect: When reaction rates are compared due to isotopic changes at loci other than the reaction center.

10.3. Origin of the primary kinetic isotope effect.

**10.3.1.**

10.3.1.1. The difference in vibrational energy between X-H and X-D is the basis for the primary isotope effect.

10.3.1.1.1. Above is shown the potential energy curve as the bond elongates (vibrates).

10.3.1.1.1.1. This curve is electronic in nature.

10.3.1.1.1.2. On this curve are much smaller energy differences that constitute vibrational and rotational states.

10.3.1.2. At room temperature >99% of the mass is in the 0 vibrational state.

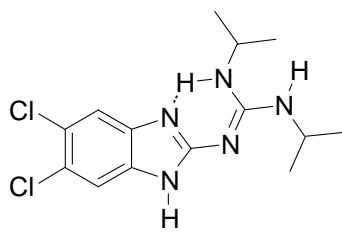
10.3.1.2.1. This energy is called the zero point energy

10.3.1.2.2. It is $1/2h\nu$ above the very bottom of the well.

10.3.1.2.2.1. Remember that ν is affected most by the difference in reduced mass.

10.3.1.3. The energy of the dissociated $X\cdot$ and $H\cdot$ versus $X\cdot$ and $D\cdot$ should be the same because the chemistry of D and H are very similar except for the arguments that include mass.

10.3.2. The vibrational energy differences can be measured by IR.

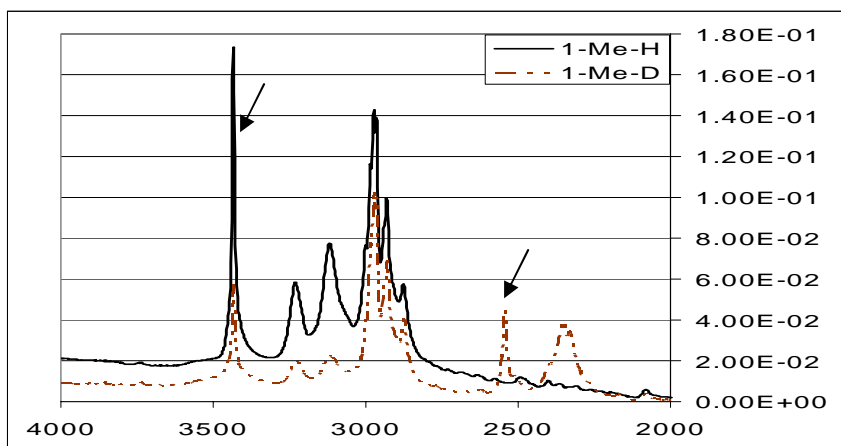


10.3.2.1.1.

KBr sample.

10.3.2.1.2. The arrows in the spectrum above indicate the IR signature of the intramolecular hydrogen bonded N-H.

10.3.2.1.2.1. 3435 cm^{-1} and 2544 cm^{-1} respectively.



10.3.3.

10.3.3.1. Above is an IR spectrum in absorbance mode.

10.3.3.1.1. The black line is the parent compound and the brown dashed line is the material after warming in MeOD for a day and pumping off the solvent.

10.3.3.1.2. Under these conditions the protic X-H exchange with D. The aprotic C-H hydrogen atoms do not exchange.

11. Refer to the potential energy curve graph above for the following argument about the PKIE.

$$11.1. \quad \Delta H_{Hzvp} = 1/2h\nu + H_{zp} = 1/2hc \frac{1}{\lambda} + H_{zp}$$

11.1.1. The zero point vibrational energy for the C-H bond exceeds the very bottom of the potential energy curve (the zero point energy) $1/2h\nu$.

11.2. From the potential energy curve graph you can see that the difference in activation enthalpies ($\Delta\Delta H^\ddagger$) will be the difference in zero point energies.

$$11.3. \quad \Delta\Delta H_{HD}^\ddagger = 1/2hc/\lambda_H + H_{zp} - 1/2hc/\lambda_D + H_{zp} = 1/2hc\left(\frac{1}{\lambda_H} - \frac{1}{\lambda_D}\right)$$

11.3.1. The IR phenomenon is conveniently expressed in terms of $1/\lambda$. (cm^{-1})

$$11.4. \quad k_{RH} = (kT/h)e^{-\Delta G_H^\ddagger/RT} = (kT/h)e^{-\Delta H_H^\ddagger/RT} e^{\Delta S_H^\ddagger/R},$$

11.4.1. Where k_{RH} is the rate of H-C bond cleavage in some rate-determining process.

$$11.4.2. \quad \frac{k_{RH}}{k_{RD}} = e^{\Delta\Delta H_{HD}^\ddagger/RT} = e^{hc/2RT(1/\lambda_H - 1/\lambda_D)}$$

11.4.2.1. The other terms basically cancel.

11.4.2.2. The sign of the exponential argument changes because the argument above was construct in reference to the bottom of the potential energy vs. r_{ab} graph, but the rate depends on difference between the zero point energy and the dissociation energy.

11.4.2.3. The argument in the exponential looks like this:

11.4.2.3.1. $-(\Delta H_{dis} - \Delta H_{HzvE}) - (\Delta H_{dis} - \Delta H_{HzvD}) = (\Delta\Delta H_{HzvHD})$: hence a positive sign for the exponential argument as in the equation above.

$$12. \quad hc/2RT(1/\lambda_H - 1/\lambda_D) = \left[\frac{(9.53 \times 10^{-11} \text{ cal} \cdot \text{s} \cdot \text{mol}^{-1} \cdot 3 \times 10^{10} \text{ cm/s})}{(2)1.98 \text{ cal} \cdot \text{mol}^{-1} \text{K}^{-1} \cdot 298 \text{ K}} \right] (3000 - 2200) \text{ cm}^{-1}$$

$$12.1. \quad = 1.94$$

12.1.1. $9.53\text{E-}11 \text{ cal}\cdot\text{s}\cdot\text{mol}^{-1}$ above is the molar Planck constant expressed in cal; it can be calculated: $h/(4.18 \text{ J/cal})\cdot N_A$

12.2.
$$\frac{k_{RH}}{k_{RD}} = e^{1.94} \approx 7$$

12.3. and
$$\frac{k_{RH}}{k_{RD}} = e^{(1144 \text{ cal}\cdot\text{mol}^{-1})/1.99 \text{ cal}\cdot\text{K}^{-1}\cdot\text{mol}^{-1} \cdot 298} \approx 6.9$$

12.3.1. This should be the maximum PKIE (primary kinetic isotope effect) by just considering vibrational effects.

12.4. This is only the first approximation

12.4.1. The maximum PKIE increases when bending vibrations are important to the reaction.

12.4.1.1. This maximum value can increase to the tune of 40.

12.4.2. The hydrogen atom can tunnel through barriers (but tends not to do so).

12.4.2.1. This effect decreases the maximum PKIE.

13. The PKIE and the Hammond Postulate!

13.1. This is the best evidence for the validity of the Hammond Postulate

13.1.1. Hammond Postulate: the transition state resembles the highest-energy stationary state in energy and structure.

13.1.2. SEE DIAGRAMS ON P. 354, 355 AND 356.

13.1.2.1. instructor explains in some detail

13.1.3. Energetically symmetrical transition states should in theory have the largest PKIE.

13.1.3.1. Zero point vibrational energy is recovered in early and late transition states due to the similarity of the transition state structures to the highest-energy stationary state.

14. The secondary kinetic isotope effect (SKIE).

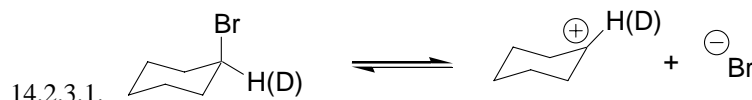
14.1. In the primary isotope effect f in the equation below was unchanged as H was substituted for D.

14.2.
$$\bar{V} = \frac{1}{2\pi c} \sqrt{\frac{f}{M_x M_y / (M_x + M_y)}}$$

14.2.1. This is because the reaction coordinate corresponded to the vibrational mode of X-H(D).

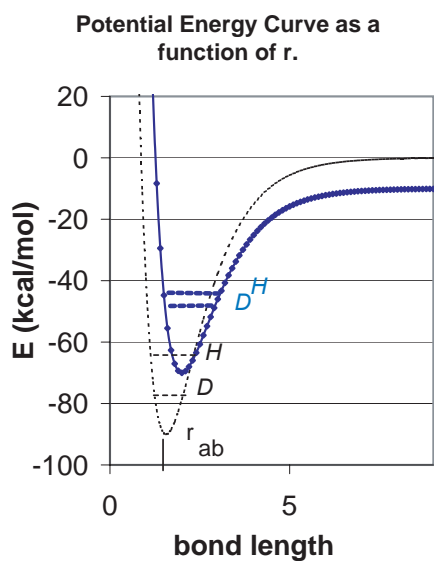
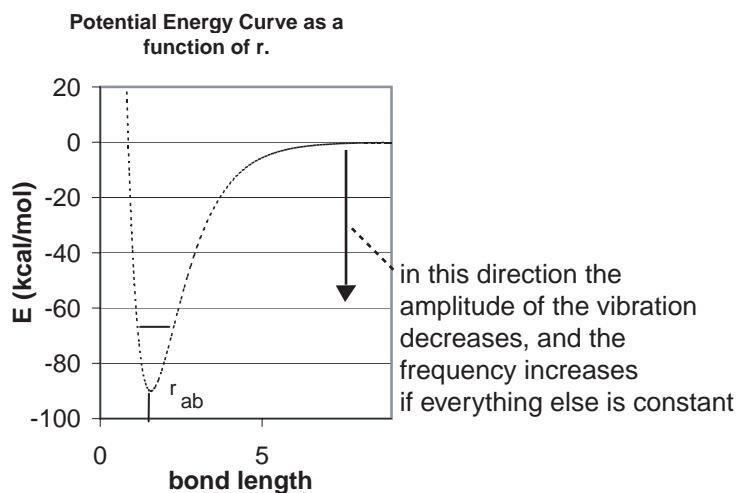
14.2.2. What if the reaction coordinate does not correspond to the vibrational mode of X-H(D)?

14.2.3. such as



14.2.3.2. Now we can't put the deuteriated and the parent molecules on the same reaction path!!

14.2.3.2.1. WHAT CAN WE SAY ABOUT THE STRENGTH of the C-H versus the C-D bond in the ground state versus the cation?

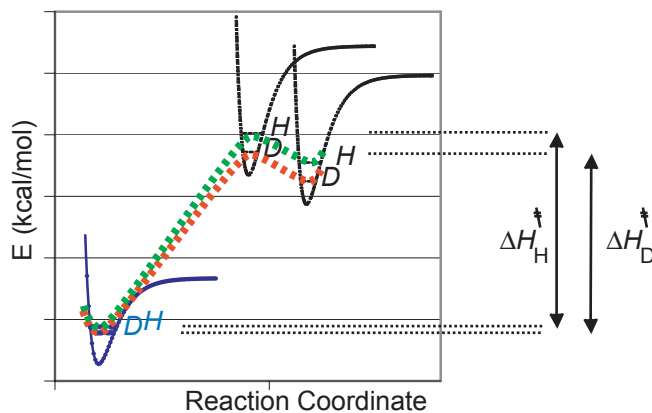


14.2.3.4.1. The blue curve is of a Morse potential that corresponds to a decreased bond strength, a decreased force constant and an increased bond length.

14.2.3.4.1.1. Morse: $V_R = D_{ab}[e^{-\alpha(r-r_{ab})} - 1]^2$

14.2.3.4.1.2. As the force constant decreases the energetic split between H and D decreases.

14.2.3.4.1.3. Now we are in position to evaluate the effect of the SKIE on the formation of the cyclohexyl cation.



14.2.3.4.2.

14.2.3.4.3. By the Hammond Postulate the T-state should be cation-like in structure and energy.

14.2.3.4.4. The C-H(D) should gain s character as the reaction occurs and thus the force constant should increase.

14.2.3.4.4.1. Hence the diagram above.

14.2.3.4.5. The reaction is associated with a larger energy barrier for H than D.

14.2.3.4.5.1. Thus the SKIE is an inverse kinetic isotope effect.

14.2.3.4.5.2. The reason it is inverse is because the bond strength of C-H(D) bond increased.

14.2.3.4.5.3. Evaluate each kinetic isotope effect on an individual basis.

14.2.3.4.5.4. Don't commit individual isotope effects to memory.

14.3. We can tell a lot about the rate determining step of a reaction by measure the PKIE and the SKIE.

14.3.1. You can say nothing about other non-rate determining processes on the reaction pathway by a study of KIE.

14.4. **Now let's talk,**

14.4.1. **What would you expect to see for a kinetic isotope effect for the isomerization of benzocyclobutane?**

14.4.1.1. Pretend this is a test question. How would go about answering it? Try it on a piece of paper.

14.4.1.2. **Getting the answer right is not nearly as important** as using your knowledge of the phenomenon to make a cogent argument and predict what you should observe if you deuteriated benzocyclobutane and compared the rate constant of the rearrangement with that of the parent.

14.4.1.3. You have to realize that whatever you do is a 'back-of-an-envelope' calculation. More accurate predictions could be likely had from better calculations.