

THE KINETIC HYDROGEN ISOTOPE EFFECT

1. Purpose

In this experiment, the isotope effect arising from substitution of deuterium for hydrogen on the rate of a reaction involving proton transfer will be investigated. The results will be interpreted in terms of the heavier isotope substituted species having a lower zero point energy.

2. Safety

Discard organic solvents to the waste solvent containers. Wear eye protection at all times in the laboratory.

3. Pre-Lab Preparation

Before starting this experiment, make sure 1) that you understand the principle of the hydrogen isotope effect and 2) that you understand how many solutions must be prepared and how to prepare them (see experimental section).

4. Introduction

4.1 THEORY

In general, isotopic replacement of atoms has an insignificant effect (although of great importance for some applications) on the chemical or physical process under consideration and this is precisely the principle behind the use of isotopic tagging in NMR for instance or radioisotope labels used as tracers in complex systems. This comes from the fact that isotope effects governed by diffusion processes go roughly as the square root of the ratio of the isotopic masses; for most common elements, this ratio is between unity and 1.1. However in the case of hydrogen and deuterium¹, since the mass ratio differs greatly from unity, isotope effects may no longer be negligible and further these effects may be used as mechanistic probes.

¹For this element, the range of isotopic masses available can be extended if one includes the radioactive atom ³H (tritium, $t_{1/2} \approx 12$ y, $m_{^3\text{H}}/m_{\text{H}} \approx 3$), the exotic atoms Mu (muonium [μ^+e^-], $t_{1/2} \approx 1.5$ μ s, $m_{\text{Mu}}/m_{\text{H}} \approx 0.1$) and Ps (positronium [e^+e^-], $t_{1/2} \approx 11$ ns, $m_{\text{Ps}}/m_{\text{H}} \approx 0.001$).

For a chemical reaction, the kinetic hydrogen isotope effect is the change observed in the rate of the reaction due to the isotopic replacement of a hydrogen atom involved in the rate-determining step of the process. The effect has been best documented for the case of proton transfer reactions. The energetic of such a reaction is shown very schematically in Fig. 1 which illustrates the variation in the potential energy of the reacting system at different stage along the reaction coordinate. In particular, the energy difference between the lowest point and the highest point of the barrier between reagent and product represents the classical activation energy of the reaction. In simple terms, the system has to be provided with enough energy (has to be activated) to overcome the height of the barrier for the reaction to occur. Since the intermolecular and inter-atomic forces are practically unaffected by a change in nuclear masses, the same potential energy curve apply for both isotopic species. However, the position of the lowest energy levels (the zero-point energy) of both the initial and the final states *does* depend upon the isotopic mass, with the lighter isotopic species having a higher zero point energy.

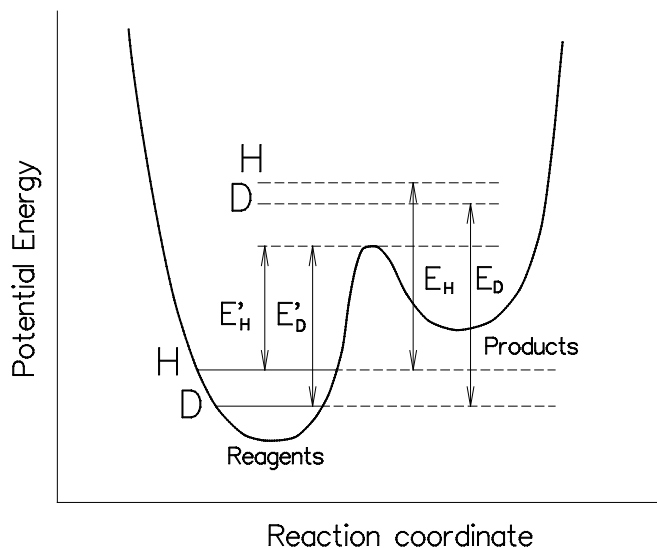


Figure 1. Schematic diagram of the potential energy profile of proton transfer reaction along the reaction coordinates; the relative position of the zero point energy corresponding to the H and D isotopes are indicated, both for the reagents and the transition state.

As a results, the activation energies E'_H and E'_D corresponding to the two isotopic species differ to a good approximation by the difference in zero

point energy as depicted in Fig. 1. Assuming an Arrhenius behaviour for the reaction, the ratio of the rate constants would then be given by:

$$\frac{k_H}{k_D} = \exp \left[- \frac{(E'_H - E'_D)}{RT} \right] \quad (1)$$

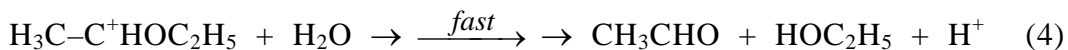
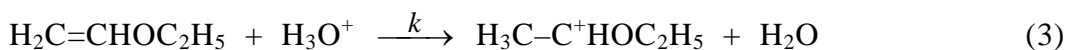
However, in a multi-step mechanism, one can expect the kinetic hydrogen effect to be the product of two terms

$$\frac{k_H}{k_D} = \left(\frac{k_H}{k_D} \right)_I \left(\frac{k_H}{k_D} \right)_{II} \quad (2)$$

where the first term $(k_H/k_D)_I$ represents the *primary isotope effect* and originates from the effect of isotopic substitution of a hydrogen atom involved in the actual bond making (or bond breaking) in the rate-determining step. The second term, $(k_H/k_D)_{II}$ accounts for the *secondary isotope effect*, which is due to the effects of isotopic substitution on the reaction rate of any other hydrogen atoms. Theory predicts a value of ≈ 10.6 for the primary isotope effect term and a value of ≈ 0.48 for the secondary term[1]. Combining these two terms, the overall effect is expected to be ≈ 5 , but experimentally lower values of ≈ 3 are observed.

4.2 HYDROLYSIS OF ETHYL VINYL ETHER.

This isotope effect will be illustrated in the present experiment by studying the kinetics of the acid catalysed hydrolysis of ethyl vinyl ether (EVE) into acetaldehyde and ethanol in aqueous medium. In the accepted mechanism, the first step is rate-determining and consists of a proton transfer to one of the vinyl carbon resulting in a carbonium center intermediate (Eqn. 3). Next, in the presence of water this intermediate rearranges and breaks apart to give the final products and regenerate a proton through a series of very fast steps (Eqn. 4).



Following the above discussion, the primary isotope effect is expected to arise from proton transfer from H_3O^+ to EVE (Eqn. 3) while the subsequent series of fast steps (Eqn. 4) involving H_2O would contribute to the secondary isotope effect.

The rate of hydrolysis of EVE has been shown to be first order in both EVE and acid concentrations with the rate law:

$$-\frac{d[\text{EVE}]_t}{dt} = k[\text{H}^+]_t [\text{EVE}]_t \quad (5)$$

where k is the second order rate constant and $[\text{EVE}]_t$ the EVE concentration at time t . As can be seen from Eqns. 3 and 4, the concentration of the catalyst H^+ (or H_3O^+) does not change over the course of the reaction and therefore the term $k[\text{H}^+]_t = k[\text{H}^+]_0 = \text{constant}$. Letting $k_1 = k[\text{H}^+]_0$, Eqn. 5 can be re-written as a pseudo-first order rate law

$$-\frac{d[\text{EVE}]_t}{dt} = k_1 [\text{EVE}]_t \quad (6)$$

which integrates readily as:

$$[\text{EVE}]_t = [\text{EVE}]_0 \exp(-k_1 t) \quad (7)$$

Equation 7 represents an exponential decay which is conveniently linearized by taking the natural logarithm of both sides

$$\ln[\text{EVE}]_t = -k_1 t + \ln[\text{EVE}]_0 \quad (8)$$

Instead of measuring the rate disappearance of EVE, one could measure the rate of apparition of one of the final products, CH_3CHO for example. Since all the steps in Eqn. 5 are much faster than the first proton transfer, one has at any time:

$$[\text{CH}_3\text{CHO}]_t = [\text{EVE}]_0 - [\text{EVE}]_t \quad (9)$$

and therefore

$$\frac{d[\text{CH}_3\text{CHO}]_t}{dt} = -\frac{d[\text{EVE}]_t}{dt} \quad (10)$$

Integration leads to

$$[\text{CH}_3\text{CHO}]_t = [\text{CH}_3\text{CHO}]_\infty [1 - \exp(-k_1 t)] \quad (11)$$

where $[\text{CH}_3\text{CHO}]_\infty = [\text{EVE}]_0$ is the concentration of acetaldehyde at completion of the reaction. Equation 11 is more conveniently processed in a linear

form obtained after some rearrangement and again taking the natural logarithm of both sides:

$$\ln([\text{CH}_3\text{CHO}]_\infty - [\text{CH}_3\text{CHO}]_t) = -k_1t + \ln[\text{CH}_3\text{CHO}]_\infty \quad (12)$$

The rate of EVE hydrolysis can be measured by following spectrophotometrically as a function of time either the disappearance of the EVE starting material at 210 – 225 nm or the appearance of the acetaldehyde final product at 270 – 280 nm.

At a given wavelength, the absorbance A_λ is related to the concentrations of the absorbing species through Beer–Lambert law

$$A_\lambda = \varepsilon_\lambda cl \quad (13)$$

where ε_λ is the *coefficient of absorption* (also called *molar absorptivity*), c the concentration and l the optical path length through the absorbing medium. Looking at the disappearance of EVE and plugging Eqn. 13 into Eqn. 8, one gets

$$\ln[(A_{\text{EVE}})_t - (A_{\text{EVE}})_\infty] = -k_1t + \text{constant term} \quad (14)$$

where the term $(A_{\text{EVE}})_\infty$ accounts for some residual absorbance present at completion of the reaction. On the other hand, if the appearance of the acetaldehyde is followed, plugging Eqn. 13 into Eqn. 12, one gets

$$\ln[(A_{\text{CH}_3\text{CHO}})_\infty - (A_{\text{CH}_3\text{CHO}})_t] = -k_1t + \text{constant term} \quad (15)$$

with the obvious notations. In either case, by plotting the left side of Eqn. 14 or Eqn. 15 versus time, one should get a straight line with slope $-k_1$ from which the second order rate constant can be calculated knowing the acid concentration, $k = k_1/[\text{H}^+]$, or more precisely, $k_{\text{H}} = k_1/[\text{H}^+]$ for the protonated acid or $k_{\text{D}} = k_1/[\text{D}^+]$ if the deuterated acid is used.

5. Experimental

The time profile of the reaction will be obtained first at 25 C for both isotopic species for a series of four H_3O^+ (D_3O^+) concentrations, then at two other temperatures at the lowest H_3O^+ (D_3O^+) concentration. The disappearance of EVE will be monitored around 215 nm using a computer controlled HP-8453 UV/VIS spectrophotometer.

5.1 SOLUTION PREPARATION

Stock solutions of HCl/H₂O and DCl/D₂O \approx 0.04 M are provided; record their exact respective concentration. Dry methanol (the “electronic grade” is adequate) and a sample of ethyl vinyl ether are also available.

Table 1. Suggested volumes to prepare a series of acid concentrations.

Soln #	Stock HCl	H ₂ O	\approx [H ⁺]/M	Stock DCl	D ₂ O	\approx [D ⁺]/M
1	1.50 ml	0.50 ml	0.03	2.00 ml	–	0.04
2	1.00 ml	1.00 ml	0.02	1.50 ml	0.50 ml	0.03
3	0.50 ml	1.50 ml	0.01	1.0 ml	1.00 ml	0.02
4	0.30 ml	1.70 ml	0.006	0.50 ml	1.50 ml	0.01

First prepare in a weighing bottle 1 ml of a 1:1 by volume EVE/MeOH solution. This is plenty since each run uses only 5 μ l of this stock solution. When not in use, keep this solution capped to prevent evaporation. Two series (H and D) of four acid concentrations are needed and are prepared directly in the UV/Vis cuvette as suggested in Table 1. If available, automatic pipettes may be used to measure some of the volumes.

5.2 DATA COLLECTION

The spectrophotometer will be set up to record the spectra at preset time intervals; the instructor will brief you on how to operate this instrument.

- Under the item **Mode**, activate **Execute Advanced Methods**; this sets a change in the interacting window panel.
- On the menu bar, click on Instrument then Setup Spectrophotometer; the pop-up window which is displayed allows you to set the sampling rate and the number of samples through various parameters. Set the wavelength range to 190 nm to 300 nm and make sure that the Tungsten Lamp button is **Off** while the Deuterium Lamp button is **On**. Set the **Run Time** and the **Cycle time** as suggested in Table 2; leave the other parameters at their defaults values. Click on **OK**.
- Prepare the acid solution in the quartz cell, cap and if necessary wait for 5 min to allow for temperature equilibration.
- While the cell is equilibrating, click on the **Blank** button to collect the baseline spectrum, the blank being the acid solution before injection of EVE.

- Inject 5 μl of EVE solution with an automatic pipette, stir quickly with the eppendorf tip, cap the cell then click on **Sample** to collect the spectra.
- At the end of the run save the data (File - Save as - Samples, give a new name of the type xxxxxxxx.sd for each run), then **clear** this spectrum (choose Edit - Clear - Samples).
- Measure the temperature of the sample at the end of the run with a digital thermocouple thermometer probe immersed in the solution in place.
- Empty, rinse with acetone and dry the cell *thoroughly* and repeat the procedure for the next solution.
- Repeat the runs with solution 4 at $\approx 35\text{ C}$ then 45 C (to obtain these values in the cuvette, the circulator should be set at $\approx 40\text{ C}$ and $\approx 50\text{ C}$, with the thermostat cooling water OFF).

Table 2. Suggested timing parameters for kinetic data collection.

Isotope	Temp./C	[Acid]/M	Run Time/s	Cycle time/s
H	25	0.03	120	6
H	25	0.02	180	10
H	25	0.01	360	20
H	25	0.006	600	30
H	35	0.006	240	12
H	45	0.006	100	5
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D	25	0.04	240	12
D	25	0.03	360	20
D	25	0.02	500	25
D	25	0.01	1000	50
D	35	0.01	360	20
D	45	0.01	180	10

6. Calculations and discussion

The data have to be recovered from the computer attached to the spectrophotometer. Unfortunately at present, the sample files will have to be retrieved under two different **Modes** to compile all the necessary information.

- To recover the timing information, go to the **Mode** Execute Advanced Methods, load the relevant sample file. Click on **Configuration Table**, then tick **out** all the proposed items except for Relative Time. Make sure the Sample/Results window is activated, then go to File - Print to File - Selected Window, then when prompted give a different file name of the type xxxxxxxx.txt for each run. This will save in plain ASCII text format the information displayed on the active window. Proceed in this way for all your data.
- Next to recover the absorbance information, go to File - Load Method, choose the “method” HDEXPT.M. Then again load one of your sample file; one window displays the spectra while the other window display a table of absorbencies at different preset wavelengths. Activate this last window, then go to File - Print to File - Selected Window and again when prompted give a file name of the type xxxxxxxx.txt, different for each run and *different from the names used in the previous step*. Process all your data in this way.
- These xxxxxxxx.txt ASCII files can be imported into any spreadsheet program. Use the **Copy** features to extract the time then the absorbance information and **Paste** it into another spreadsheet (weighted least-squares or of your own design) which processes the data according to Eqn. 14.

For the 25 C runs, following Eqn. 14 obtain and tabulate the values of k_{1H} and k_{1D} for each of the acid concentration then calculate the corresponding second order rate constants k_H and k_D and report the average value for each isotope. From these data, calculate and comment on your observed hydrogen isotope effect.

Process similarly the data obtained at different temperatures, *i.e.*, first tabulate the values of the pseudo-first order rate constant, then calculate the corresponding second order rate constants. Comment on the isotope effect observed. Next, to calculate the Arrhenius activation energy E_H for the H reaction (or E_D for the D reaction), depending on the quality of the data,

1) one can obtain $E_{H(D)}$ from the slope of the Arrhenius plot of $\ln(k_{H(D)})$ versus $1/T$ (slope = $-E_{H(D)}/R$), or

2) if the scatter is too large, one can use the temperature results pairwise according to:

$$\frac{k_H(T_1)}{k_H(T_2)} = \exp \left[-\frac{E_H}{R} \left(\frac{1}{T_1} - \frac{1}{T_2} \right) \right] \quad (16)$$

then E_H is taken as the average of the three values obtained; E_D is obtained in the same way using Eqn. 16 in which the subscript H is replaced by D.

In principle, the activation energy E_D for the D reaction can also be calculated from

$$\frac{k_H(T_1)}{k_D(T_1)} = \exp \left[-\frac{(E_H - E_D)}{RT_1} \right] \quad (17)$$

Compare the two values of E_D obtained; why are they different?

Discuss your results in terms of the difference in zero point energies between the two isotopes. What are the shortcomings of the simple model shown in Fig. 1 and more precisely what is the meaning of the energies labelled E_H and E_D compared to E'_H and E'_D ? Is the present model adequate to account for the effects observed in this experiment? Propose a detailed mechanism for the series of fast steps in Eqn. 4. The ethyl vinyl ether commercially available contains 0.1% KOH. What is the role of this additive and to what extent is it affecting the acid concentrations used in the present experiment?

7. References

- [1] P. McGuigan, R. Eliason, B. Anderson and B. Botch, *J. Chem. Ed.* **64**, 718 (1987).
- [2] R.P. Bell, *The Proton in Chemistry*, 2nd Ed., Cornell University Press, Ithaca, N.Y. (1973).
- [3] M.M. Kreevoy, *J. Chem. Ed.*, **41**, 636 (1964).
- [4] J.M. Williams, M.M. Kreevoy, *Adv. Phys. Org. Chem.*, **6**, 63 (1969).
- [5] E.K. Thornton, E.R. Thornton, in *Isotope Effects in Chemical Reactions*, C.J. Collins, N.S. Bowman Eds., Van Nostrand Reinhold, N.Y. (1970), chapter 4.

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