

8. Investigating the temperature dependence of drug decomposition

8.1. Introduction

During this practice we study the pseudo first-order hydrolysis reaction of acetylsalicylic acid. The rate constant of a first-order reaction can be written as:

$$k = \frac{1}{t} \ln \frac{z}{z - x} \quad (8.1)$$

where t is time, z is the initial concentration of the reagent, x is the concentration of the product at time t .

The reaction rate depends on temperature, which is stated in the *Arrhenius law*:

$$\frac{d \ln k}{dT} = \frac{E}{RT^2} \quad (8.2)$$

after integration:

$$k = Ae^{-E/(RT)} \quad (8.3)$$

and

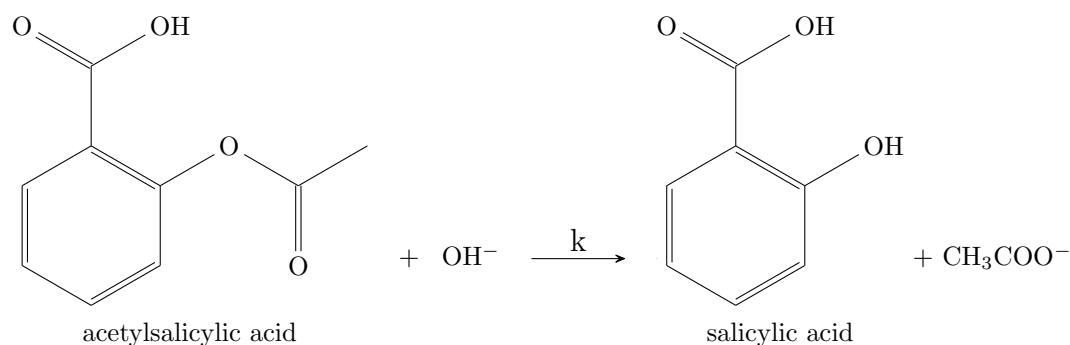
$$\lg k = \lg A - \frac{E}{2.303RT} \quad (8.4)$$

A is the preexponential factor, E is the activation energy, and R is the universal gas constant ($R = 8.314 \text{ J/Kmol}$). The factor 2.303 is the conversion from \ln to \lg . Activation energy can be obtained graphically if we take the slope of the function $\lg k - 1/T$ and multiply it by 2.303×8.314 . The dimension in this case for E is J/mol . If we measure k on two different temperatures (k_1 and k_2 on T_1 and T_2 temperature), activation energy can be calculated as follows:

$$E = 2.303 \times 8.314 \lg \frac{k_1}{k_2} \frac{T_1 T_2}{T_1 - T_2} \quad (8.5)$$

8.2. Practice procedures

Alkaline hydrolysis of acetylsalicylic acid (Fig. 8.1) is a pseudo first-order reaction. The reaction is quite slow on room temperature, therefore we conduct our measurements at a higher temperature. To determine the rate constant k , we need to know the change in concentration of the reactants or the products as a function of time. In this practice, we will use spectrophotometry after forming an Fe^{3+} salicylate complex by adding FeCl_3 to the samples. The complex has a deep violet color, and



8.1. ábra. Alkaline hydrolysis of acetylsalicylic acid.

its absorbance is directly proportional to the concentration of the complex, therefore to the concentration of the product salicylate as stated by *Lambert-Beer's law*:

$$A = \epsilon lc \quad (8.6)$$

where A is absorbance, ϵ is the molar decadic absorption coefficient, l is the length of the solution block the light is passing through, and c is the concentration. We take known volumes of samples from the alkaline reaction vessel, and suddenly decrease $[\text{OH}^-]$ and temperature by adding NaOH and putting the samples on ice. If the measured absorbance is above 2 A.U., dilution is necessary, since over this value the relationship between c and A is not linear anymore. To determine the product concentration at $t = \infty$ (which equals to the reactant concentration at $t = 0$), we take samples at the end of the practice. We carry out the measurements at two different temperatures, determined by the instructor (usually 313 and 353 K).

Pulverize an *Aspirin* tablet in a mortar with the help of a pestle, dissolve it in a small amount of deionized water, then filter it into a 100 cm³ measuring flask, and fill it up to 100 cm³. This will be the stock solution. The stock solution obtained in this way will be most likely saturated¹

Starting and following the reaction:

- (a) Determining the initial concentration z of acetylsalicylic acid. Pipette 2-2 cm³ sample from the stock solution into two Erlenmeyer flasks with bottlecaps (low and high temp.), and add 3-3 cm³ 0.25 M NaOH solution to them. Put them into the two thermostats after labeling them. At the end of the practice we stop the reaction. It should be complete, but we should treat these solutions as the others to rule out any artifacts. „Stop the reactions” by adding 2-2 cm³ 0.25 M HCl solution and 3-3 cm³ FeCl₃, then fill the flasks up to 100 cm³ with deionized water.

¹An *Aspirin* tablet has 500 mg acetylsalicylic acid in it, and its solubility in water is 2 - 4 g / L, depending on temperature.

- (b) Determining concentration x at time t . Put one half of the remaining stock solution into an Erlenmeyer and the other half into another Erlenmeyer flask. Close the flasks, label them, and put them into their respective thermostats. Add 5 cm³ buffer solution (ask the technician), and start a stopwatch. By adding the buffer solution the reaction starts ($t = 0$). Without taking out the flask, take 2 cm³ samples from them at 15, 20, 25, 30 and 35 minutes after the reaction has started, and put them into separate, labeled 25 cm³ measuring flasks you prepared beforehand. Prepare them by adding 0.5 cm³ 0.25 M HCl solution (this will stop the *alkaline hydrolysis*), and 0.5 cm³ 0.1 M FeCl₃ solution (to form the complex and make the product visible for spectrophotometry). Fill the remaining volume in the 25 cm³ flasks with deionized water. Start the two reactions by shifting one by 1 – 2 minutes, so you don't have to take samples at the same time from the two reactions.

Measuring absorbance and calculating concentration. Both the initial and the instantaneous concentration at time t will be measured spectrophotometrically. Find the users manual next to the instrument, or ask the instructor to help. To calculate the concentration from absorbance use the factor $b = 8.3 \text{ (mol/dm}^3\text{)}/\text{AU}$. This is the concentration of the theoretical solution, whose absorbance is 1 AU, if $d = 1 \text{ cm}$, where d is the length of solution block in the path from source to detector.

8.3. Results to submit

1. Measured and calculated data in table (use table 8.1 as reference).
2. Calculate the rate constants (table 8.2.) for both temperatures, and calculate standard deviation².
3. From the temperature dependence of the rate constant, calculate the rate constant for 20 °C-on (293 K) graphically by plotting $\lg k$ as a function of $1/T$.
4. Calculate E and A by substituting into the integrated form of the Arrhenius equation:

(a) $E \text{ [kJ mol}^{-1}\text{]}$

(b) $\lg A \text{ [s}^{-1}\text{]}$

(c) $A \text{ [s}^{-1}\text{]}$

²Standard deviáció, $s = \sqrt{\frac{\Sigma(x_i - \bar{x})^2}{n-1}}$

8.1. táblázat. Measured and calculated data.

T = ... K, $z = \dots \text{ mg}/100 \text{ cm}^3$

reaction time, s	dilution	A	x, mg / 100 cm ³	(z-x), mg / 100 cm ³	k , s ⁻¹
...

8.2. táblázat. Temperature dependence of the rate constant.

T, K	1/T	\bar{k} (average), s ⁻¹	lg k	standard deviation
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