Class Projects in Physical Organic Chemistry: The Hydrolysis of Aspirin - Supplemental Material

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Experimental Procedure

Each student determines the rate constant for the hydrolysis of aspirin at three different pH values. These determinations are done simultaneously in one lab period. A solution of aspirin in ethanol (note the concentration from the stock bottle) and solutions of the various buffer components are available in the lab. Strong acids and bases are used in preparing the buffer solutions, therefore safety glasses, a lab coat and disposable gloves are used as personal protection.

To produce a solution of the required pH, mix the buffer components in the ratios noted in the table. Use a graduated cylinder, and don't be too exact. Slight variations in the buffer makeup actually increase the number of pH readings available.

Standardize a pH meter using the 7.41 and 10.4 buffers supplied. The pH readings in the table are approximate - you will need to measure the pH of your buffer solution (to 2 decimal places) before you begin the reaction

Table 1: Buffer Compositions for Different pH Values

mL of 0.20 M Component Solution Used to Make 100 mL of Buffer (pH is approximate)								
HCl	KCl	AcOH	KH_2PO_4	H_3BO_3	NaOH	H_2O	pH	time
75	25						1.0	12
10	25					65	1.6	15
2	25					75	2.3	15
		100					2.8	15
		10				90	3.2	15
		50			10	40	4.0	12
		50			25	25	4.5	12
		50			40	10	5.1	12
		50			48	2	5.9	12
			50		10	40	6.2	12
			50		25	25	6.7	10
			50		40	10	7.2	10

			50		50		8.1	10
				50	10	40	8.6	10
				50	25	25	9.2	5
				50	35	15	9.6	3
				50	42	10	10.1	2
				50	50		10.6	2

The hydrolysis will be studied at 60 °C. To prepare a solution for hydrolysis, transfer about 97 mL of your buffer (*ie* below the mark) to a 100 mL volumetric flask. Thermally equilibrate the buffer by placing it in the water bath for at least 20 min. Remove the flask from the bath, quickly add 1.00 mL of the aspirin solution, start timing the reaction, and bring the solution up to the mark with buffer. Mix the reaction mixture well, and return it to the water bath.

Begin to take absorbance readings. To take a reading, open the flask, and use a transfer pipette to remove about 3 mL of solution into a quartz cuvette. Measure the absorbance in an Ultrospec set at 298 nm, using a reference of distilled water in the same cuvette. When reading the absorbance, take the time when the absorbance was read, not the time the sample was removed. Return the sample to the reaction mixture, and periodically shake the flask. Continue to record the absorbance of the solution for the remainder of the period, or until the absorbance is greater than 1.4.

The frequency with which you should take absorbance readings is given in the "time" column in the previous table. The times are in minutes. The cuvette must be cleaned and dried between readings. After returning the sample to the reaction flask, rinse the cuvette well with distilled water, followed by methanol. The methanol is then removed with a gentle stream of air.

The required Añ reading may be taken by one of two methods. Either a) wait 24 or more hours, and then take an absorbance reading or b) assume all of the aspirin will be hydrolyzed, and calculate an Añ based on salicylic acid/salicylate ion having a molar absorptivity of 3470 at 298 nm.

Report

Within one week of doing the experiment, submit your results to the laboratory coordinator for posting. Only the measured pH and rate constants (in s^{-1}) will be posted. The combined results will be available on the notice board in the lab, and on the department's web page.

Compute the rate constants for the pH values that you studied. Prepare a plot of log(k) *vs* pH for a class set of data (a minimum of 18 rate constants over the full pH range shown in the table). Describe the mechanism of hydrolysis at the different pH ranges. Discuss how the experiment could be improved.

Instructor Notes

1) The hot water bath is prepared from an 18 x 12 x 12 polypropylene tank (Nalgene #14200-0015) and a variable temperature immersion heater (Haake C1). The immersion heater may be connected to a

timer to allow the heater to come on automatically. About 90 minutes is required to thermally equilibrate the hot water bath.

2) The temperature control for the heater may be taped (or screwed!) down to prevent accidental temperature adjustment. The temperature of the bath will remain within 0.2 °C of the set temperature, even over a term.
3) The heated buffer solution should be used to measure the pH. Measuring the pH at room temperature does not affect the overall shape of the pH rate profile, but does introduce errors in the measurement of the pH of the more basic solutions.
4) An Ultrospec 2100 pro uv/visible spectrophotometer is available. Two quartz cuvettes are available for the students - please take care with the cuvettes as they are expensive!
5) A 1.00 mL pipetter, with tips, is available for dispensing the aspirin solution.
6) Two students at a time can work on this experiment. Efficient planning and cooperation are needed to make the best use of the spectrophotometer.
7) A determination of the actual $A_{\tilde{n}}$ is preferable, however this can take several days for the slower reactions. The use of a calculated $A_{\tilde{n}}$, while not experimentally valid, still gives remarkably accurate results. The calculated $A_{\tilde{n}}$ will be about 1.92.

Preparation Notes

This experiment requires a moderate amount of solution preparation. There is a total of nine solutions that need to be made (8 buffers and aspirin). Extra supplies of the buffer solutions must be available.

Buffers: The pH 7.41 and 10.4 buffer standards can be made from commercially available packages (Fisher Scientific). The remaining buffer components can be prepared as shown in table 2.

Table 2: Preparation of the Buffer Components

Compound	Amount required to prepare 1.00 L of a 0.20 M solution.
HCl	0.2 *N* solutions of HCl may be purchased commercially

KCl	Use 14.9 g of solid KCl.
Acetic acid	Use 12.0 g of glacial acetic acid.
KH_2PO_4	Use 27.2 g of solid K_2PO_4.
H_3BO_3	Use 12.4 g of solid H_3BO_3.
NaOH	Use 8.00 g of solid NaOH

Aspirin: Accurately weigh 1.00 g of aspirin, and dissolve in 100.0 mL of 100 % ethanol. Note the exact concentration of aspirin on the stock bottle.

CAS Registry Numbers

Acetic acid, 108-24-7; aspirin (acetylsalicylic acid), 50-78-2; boric acid, 10043-35-3; hydrochloric acid, 7647-01-0; potassium chloride, 7447-40-7; potassium dihydrogen phosphate, 7778-77-0; sodium hydroxide, 1310-73-2; water, 7732-18-5.

Spreadsheet Template

This Excel worksheet (aspirin.xls) does the calculation of the rate constant for one pH value at a time. The data analysis tools must be installed to use this worksheet. Open the worksheet in Excel, move the selector to B3, and enter the pH of the solution studied. Move to E3 and enter the calculated Añvalue for the reactions.

Move the selector to A6, and enter the time and absorbance data. The time data should be entered in minutes. The worksheet calculates the rate constants in units of s^{-1}, even though the time data is entered in minutes. It is easier to enter one column of data, and then the second (starting at B6), since the selector moves down when the enter key is pressed. The data set is (relatively) small, and it should be easy to notice mistakes in data entry.

Once the data has been entered, click on Tools/Data Analysis. Select "Regression" and click "OK". This will open the appropriate dialog box. Under the input part of the box, enter the cells that hold your data(x-axis is A6:end of data, y-axis is C6:end of data). The number of data points between the two columns must be the same. If necessary, select cell J1 as the output range. *Do not change the output range from cell J1!* Click "OK", and then click "OK" again to overwrite any old linear regression data. This must be done, or the line on the graph will not match the data entered. This will calculate the regression, and transfer the rate constant, the error in the rate constant and the r^2 value to the appropriate place on the worksheet. Click the printer icon to print the worksheet and the graph.

To start a new calculation, select the region A6:B17 (only!), and hit the delete key. This worksheet does not produce the graph of k *vs* pH. That must be done by hand, or another graphing program.