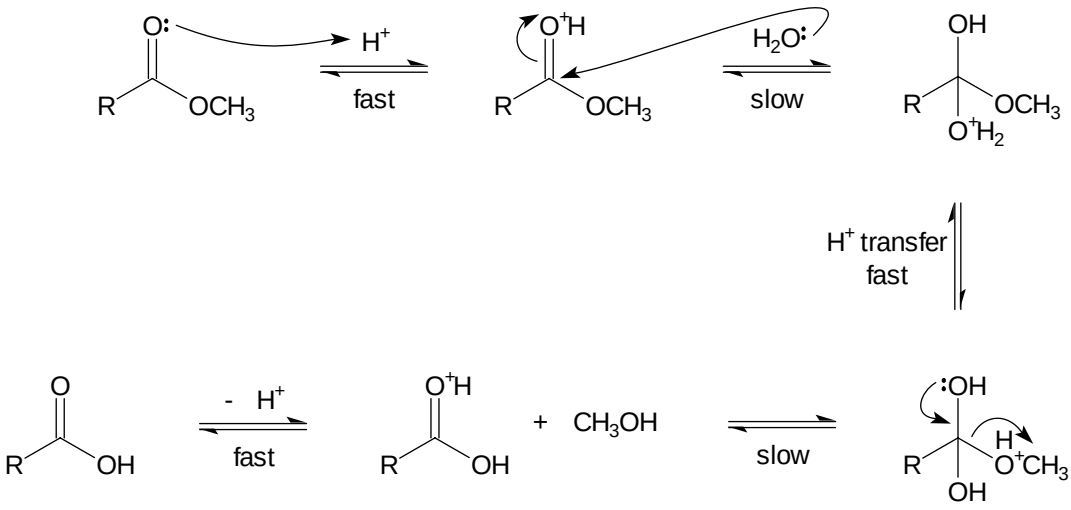
Experiment 35

Catalysis: The pH-Rate Dependence of the Hydrolysis of Aspirin

Esters are susceptible to catalytic hydrolysis by both aqueous acids and bases. The possible mechanisms are given below:



If the proton source is hydronium (H_3O^+) the catalysis is termed *specific acid* catalysis. The source of the proton is from a dissociated acid, and the substrate (the ester) is protonated in the transition state of the reaction. The undissociated acid (if present) does not appear in the transition state. Rate equations may also be used to describe the catalysis. For specific acid catalysis, the observed rate constant, k_{obs} is described by:

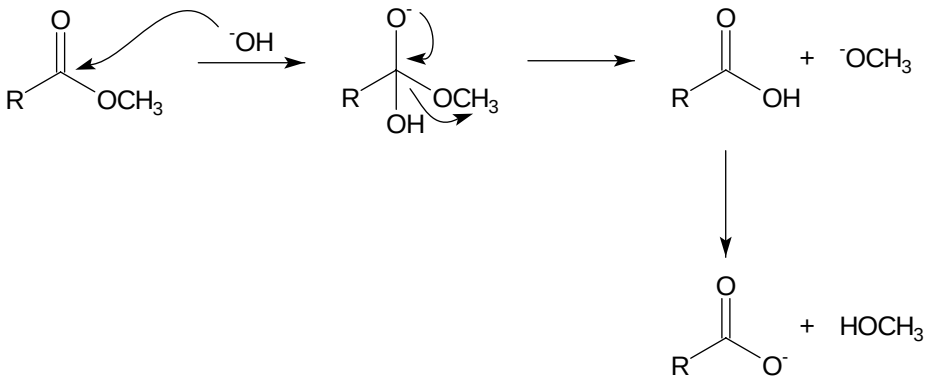
$$k_{obs} = k_0 + k_H [H_3O^+]$$

where k_0 is the rate constant for the uncatalyzed process and k_H is the rate constant for the acid catalyzed process. Note that there is no term in the equation for any undissociated acid present in the reaction mixture.

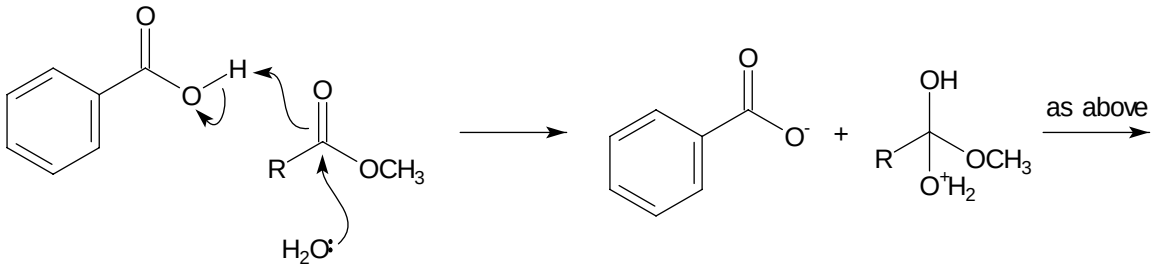
A similar situation exists for basic hydrolysis (the mechanism is on the top of the next page). When the base is hydroxide (OH^-), the catalysis is termed *specific base* catalysis. The ultimate source of the base *is* hydroxide in the reaction mixture, and the substrate is attacked by the hydroxide in the transition state of the reaction. There are no other bases *ie* the conjugate base of an acid, in the transition state. The observed rate constant, k_{obs} for the reaction is described by:

$$k_{obs} = k_0 + k_{OH} [OH^-]$$

where k_0 is defined as above, and k_{OH} is the rate constant for the hydroxide catalyzed process.



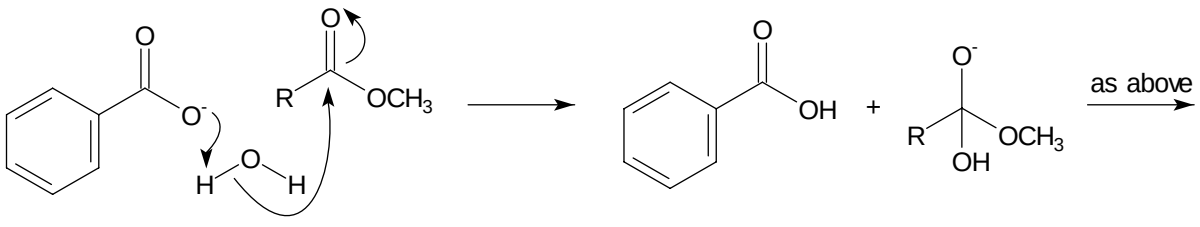
Catalysis also occurs where an *un*dissociated acid exists in the transition state of the reaction. This is termed *general acid* catalysis. A typical mechanism involving an undissociated acid (benzoic acid) is shown below. The transfer of the proton to the substrate occurs in the transition state of the reaction.



The equation for the observed rate constant for this type of reaction includes a term for each undissociated acid (HA) in the reaction.

$$k_{obs} = k_0 + k_H [H_3O^+] + \sum_{HA} k_{HA} [HA]$$

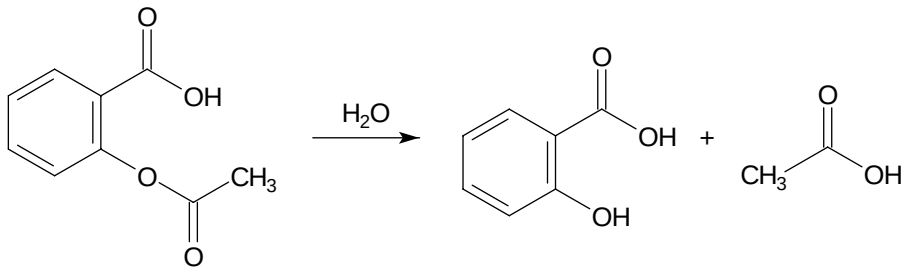
Catalysis that involves the conjugate base of an acid in the transition state of a reaction is termed *general base* catalysis. Catalysis of this type often occurs in enzymatic hydrolyses. A mechanism for this type of catalysis is shown below. What is occurring in this mechanism is the conjugate base of benzoic acid is deprotonating water, which is simultaneously attacking the substrate. This is more accurately called general base assisted nucleophilic attack.



Analogous to the general acid catalysis, the equation for the observed rate constant for general base catalysis includes a term for each conjugate base in the reaction.

$$k_{obs} = k_0 + k_{OH}[OH^-] + \sum_B k_B [B]$$

Aspirin **I**, acetylsalicylic acid, is an ester. The equation for its hydrolysis to salicylic and acetic acids may be written very simply.



The exact mechanism of hydrolysis is a bit more difficult to describe, since the hydrolysis of aspirin may occur by one or more of the mechanisms described above. It is the purpose of this experiment to determine what effect a change in pH (*ie* a change in $[H_3O^+]$ or $[OH^-]$) will have on the rate of aspirin hydrolysis. Measurement of the observed rate constant over a large pH range will produce a pH-rate profile. Different regions on this pH-rate profile will correspond to different types of catalysis, and the catalysis observed can be related to different mechanisms of hydrolysis. Therefore by studying the pH-rate profile, the hydrolysis of aspirin can be understood over the full pH range.

It can be shown that the hydrolysis of aspirin is pseudo-first order under the conditions used. Thus the equation:

$$\ln (A_{inf} - A_t) = - k t$$

where A_{inf} is the absorbance at infinite time, A_t is the absorbance at time t, and k is the pseudo-first order rate constant, can be used to describe the kinetics. A plot of $\ln(A_{inf} - A_t)$ *vs* t should be linear with a slope of -k.

Experimental

To keep a relatively constant pH while studying the hydrolysis of aspirin, the use of buffers is necessary. The following buffer components are available, all in 0.20 M concentrations: hydrochloric acid, potassium chloride, acetic acid, potassium dihydrogen phosphate, boric acid and sodium hydroxide. To produce a solution of the required pH, mix the buffer components in the ratios noted in the table (use a graduated cylinder). The pH readings listed are approximate, you will need to measure the pH of your buffer solution (2 decimal places) before you begin the kinetics.

You may wish to prepare the buffers ahead of time, and store them (well sealed!) until needed. Also available will be a solution of aspirin in ethanol of known concentration.

mL of 0.20 M Component Solution Used to Make 100 mL 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 98 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, add 1.000 mL of the ethanolic 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, unstopper the flask, and use a transfer pipette to remove about 3 mL of solution into a 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 acetone. The acetone is then removed with a gentle stream of air. This last step is very important, since acetone absorbs at 298 nm any residual acetone will affect your reading.

The required A_{inf} 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 A_{inf} based on salicylic acid/salicylate ion having a molar absorptivity of 3470 at 298 nm.

The work in this experiment must be shared. Each student must do a minimum of 6 pH values. It is possible (necessary?) to do more than one pH value at a time. Plan your work to get the most of your lab time.

Report

Compute the rate constants for the pH values you studied. You may simply obtain the k & pH values from the other students. Prepare a plot of k *vs* pH. Describe the mechanism of hydrolysis at the different pH values.

Reference

1. Most textbooks on physical organic chemistry will have a section on catalysis. The major literature source for this experiment is: Edwards, L.J. *Faraday Transactions* **1950**, 723. A copy of this reference is available, the original is getting rather shopworn.