AN NMR ANALYSIS OF THE HYDROLYSIS OF α-BROMOPROPIONIC ACID

by

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Submitted in partial fulfillment of the
requirements for Honors
in the Department of Chemistry

UNION COLLEGE

June, 1986

ABSTRACT

The kinetics of hydrolysis of α-bromopropionic acid were investigated at 80° C and a constant pH of 3.3. An average first order rate constant of 4.74×10^{-3} min^{-1} was determined. This hydrolysis reaction has been studied by several workers. It is unique in that the reaction proceeds through inversion reactions, the first involving the carboxylate ion. This paper covers the first study where the pH of the system was maintained constant. The design of an inexpensive pH-stat for this purpose is given. The experiment and/or data lend themselves useful for treatment in physical chemistry where the students must gather data in a short time and interpret the results. Racemic α-bromopropionic acid is used and the reaction is followed using NMR spectroscopy.

DEDICATION

This work is dedicated to Professor John R. Sowa, my research advisor, whose friendship, guidance, warmth, and support mean so very much to me. Thanks "Dad".

ACKNOWLEDGEMENT

I would like to acknowledge the following people; Professor Jagdish Gajjar, Stan Leroy, Jack Hogle, and Douglas Steele, for their help in the design and development of the pH stat system; without their efforts, this work would not have been possible.

I would also like to thank Dr. J.R. Sowa for his helpful observations and suggestions.

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INTRODUCTION

Many studies[1,2] have investigated how substituents that are alpha to the place of nucleophilic substitution affect both the kinetics and the mechanism of substitution. These studies have been of importance in determining general laws relating the mechanism involved to the structure of the reacting compounds and the conditions of the reaction.

This project which deals with the kinetics of hydrolysis of α-bromopropionic acid was intended to provide a college-level experiment dealing with reaction kinetics, mechanisms, and their dependence upon conditions such as pH. The hydrolysis of α-bromopropionic acid is, of course, dependent upon pH due to the nature of the carboxyl group. At low pH, the major form of the species present is the undissociated acid. As the pH rises, more α-bromopropionic acid dissociates to the α-bromopropionate anion. The kinetics of the acid itself versus the anion will differ.[1]

Another goal of this project was to design and employ an inexpensive pH stat system (see Experimental, page 3). Briefly, this system maintains a constant pH in the reaction mixture by periodically adding base. The hydrolysis of α-bromopropionic acid produces lactic acid and its progress can be followed easily by nuclear magnetic resonance (NMR) spectroscopy. The disappearance of 2-bromopropionic acid and the appearance of lactic acid can be monitored versus time.

As already stated, the structure of the molecule and the nature of substituents adjacent to the substitution site greatly affects the kinetics and mechanism of a reaction. That is, kinetics and mechanisms are dependent upon steric effects, inductive effects, and neighboring group effects. This reaction is sensitive to these effects.

Thus it was the purpose of this research to examine the hydrolysis of α-bromopropionic acid at a series of different pH values. The first set of reactions were run at a constant pH of 3.3. Later, different pH values will be explored.

EXPERIMENTAL

A: Synthesis

1. Methyl 2-Bromopropanoate

Step 1: Preparation of 2-Bromopropionyl Chloride

Approximately 0.45 mole (40.5 mL) of 2-bromopropanoic acid (bp 203.5°) and a 4:1 volume excess (160 mL) of thionyl chloride (bp 79°) were refluxed for approximately 90 minutes. After the excess thionyl chloride was removed by distillation, the 2-bromopropionyl chloride (bp 131-3) was distilled. Yield of the product was 82% (37.4 mL). An NMR spectrum with a quartet centered at 4.7 ppm and a doublet centered at 1.9 ppm agreed with the spectrum published in "The Aldrich Library of NMR Spectra".[3] All of the NMR spectra in this project have been run on a Hitachi Perkin Elmer High Resolution NMR Spectrometer, Model R-24A.

Step 2: Reaction of 2-Bromopropionyl Chloride and Methanol

The acid chloride was reacted with a 2:1 volume excess (75mL) of methanol (bp 65°) to produce the methyl ester. Yield of the methyl ester was quantitative. Unreacted methanol was removed by distillation. An NMR spectrum with a doublet at 1.8 ppm, a singlet at 3.8 ppm, and a quartet at 4.3 ppm agreed with the Aldrich spectrum.[4]

2. Methyl 2-(p-Nitrophenoxy)propanoate:

Step 1: Preparation of Potassium p-Nitrophenol:

Approximately 0.1 mole (13.91g) of p-nitrophenol was reacted with 0.1 mole (5.61g) of potassium hydroxide in water. The resulting crystals were dried in a vacuum desiccator, with phosphorus pentoxide as the drying agent.

Step 2: Reaction of Potassium p-Nitrophenolate and Methyl 2-Bromopropanoate:

Equimolar quantities (0.1 moles each) of methyl 2-bromopropanoate (11.1mL) and potassium p-nitrophenolate (17.7g) were refluxed for about 2 hours in acetonitrile. Potassium bromide, which precipitated out of solution, was removed by filtration. After removal of the acetonitrile by distillation, a whitish solid (21g) remained.

Purity of the product was checked by thin-layer chromatography. The plates were silica gel and the developing solvent was methylene chloride. The TLC's showed two spots: one due to methyl 2-(p-nitrophenoxy)propanoate(Rf value = 0.42) and one due to p-nitrophenol (Rf = 0.62).

Separation of the mixture was achieved by washing the solid product with water. Percent yield of the product was 85% (19.1g).

3. <u>2-(p-Nitrophenoxy)propanoic</u> <u>Acid</u>:

Approximately equimolar quantities (0.03 mole) of the 2-bromopropanoic acid (2.7 mL) and potassium p-nitrophenolate (5.3g) were refluxed for about 2 hours. Potassium bromide precipitated from the solution.

To check the purity, a TLC was run on the product mixture, employing the same TLC conditions as in part A.2. The TLC plate showed three spots: one each from potassium p-nitrophenol (Rf=0.62), and 2-bromopropanoic acid(Rf=0.09) and one from 2-(p-nitrophenoxy)propanoic acid (Rf=0.38).

An ultraviolet spectrum of the product was compared to an ultraviolet spectrum of pure p-nitrophenol. Both spectra looked similar. Base was added to both samples and the resulting pure p-nitrophenol spectrum showed a bathochromic shift whereas the product did not, indicating the product is not a phenol. The acid ether has λ maxima (methanol) values at 227.9 nm, 308 nm, 314 nm, and 422 nm. The p-nitrophenol has λ maximum (methanol) values at 240 nm, 310 nm, and 410-420 nm. All of the ultraviolet spectra were run on a Perkin-Elmer Lambda 3B UV/VIS Spectrometer.

The separation technique employed was that of Perron, Minor, et al.[5] Their technique consisted of acidifying the mixture to pH 2, extracting with ether, extracting the ethereal solution with 5% aqueous sodium bicarbonate, and then acidifying the extracts after removal of the ether.

B: Apparatus

The apparatus employed in this project was devised to maintain, through the addition of base, a constant pH in the reaction mixture. The apparatus can be divided into three parts: the delivery system, the electronic components that sense pH changes and activate the delivery system, and the reaction vessel itself.

The delivery system consists of a peristaltic pump, tygon tubing, and a buret. The buret measures the amount of liquid being delivered into the reaction vessel. On top of the buret is a drying tube with calcium chloride, to absorb water from the air, and sodium hydroxide, to absorb any carbon dioxide from the air, thus protecting the sodium hydroxide titrant solution. The peristaltic pump forces predetermined amounts of liquid from the buret, through the tubing, and into the reaction vessel. The tygon tubing simply serves as a conduit for the base being delivered from the pump into the reaction vessel.

The pH sensing component of the apparatus consists of a pH meter, a combination glass-pH electrode, a main control box, an AC relay, a Variac, and a rectifier. The apparatus functions in the following manner: a pH electrode senses the pH of the reaction mixture. It controls the voltage input of the pH meter which then controls an electronics gate. Until a predetermined pH is read by the meter, the gate will be open, and will allow the system to add base. If base is needed, then the control box activates an AC relay. The voltage output of the AC relay is regulated by a Variac. A rectifier converts the AC voltage to DC. The DC input activates the peristaltic pump and determines the sweep of the motor driving the pump.

The pump's rate of base addition depends upon three parameters of the main control box: the pulse width, frequency, and DC voltage. The pulse width controls how long the peristaltic pump runs to squeeze liquid through the tygon tubing. Thus, a short pulse width delivers little liquid each time, whereas a longer width delivers more liquid. The frequency parameter controls how often liquid is delivered into the reaction vessel.

The reaction vessel is a 180 mL beaker with a rubber stopper in its mouth to serve as a covering. The rubber stopper has four ports in it: one for the pH electrode, one for a thermometer, one for a pipet to withdraw samples from, and one to hold a U-tube which delivers base into the reaction vessel.

To achieve a constant reaction vessel temperature (80 ° C), a heating motor was used to heat a five gallon (20 L) water bath. A second, smaller vessel contained the reaction vessel itself. Copper tubing attached to the heater passed from the large vessel into the small vessel. (see Appendix). To reduce evaporation of the water, aluminum foil covered cardboard was put on the vessels being heated.

This whole system depends upon the measurements of pH of the reaction mixture as the reaction proceeds. Thus, it is imperative to have a reliable pH electrode. The electrodes employed have been combination glass-pH electrodes. Certain problems occurred with these electrodes because of the high temperature solutions they were immersed in. At this high temperature, some of the potassium chloride crystals will dissolve and flow around inside the electrode. Once the solution cools back down to room temperature, the crystals will reform; some may block the ion junction causing the electrode to function improperly, and give an erroneous pH reading. This did not prove to be a difficulty, however, since the electrode would function properly at 80° C.

C: Technique of the Runs

A 10% by weight solution of α-bromopropionic acid was equilibrated at 80° inside the reaction vessel. Sodium hydroxide (0.482N) was added over a period of 90 minutes using the pH stat system. At time intervals of 2,5,7,10,15,20,25,30,40,50,60,75,and 90 minutes after the start of the reaction, 2 mL aliquots were withdrawn. These samples were acidified with a few drops of 12N hydrochloric acid and then iced until analyzed by NMR spectroscopy. This procedure of acidifying and then icing quenches the reaction.

D: Standardization of Base

The sodium hydroxide solutions were standardized with potassium acid phthalate that had been dried in an oven at 110° for at least 1 hour. Masses of the dried potassium acid phthalate were determined to four decimal places by a Mettler analytical balance.

RESULTS and DISCUSSION

A: Difficulties

As with any experimental work, there were several difficulties encountered in this project. These difficulties can be grouped into two categories: synthesis and separation difficulties, and equipment problems.

The first difficulty occurred with the synthesis and separation of methyl 2-(p-nitrophenoxy)propanoate. This ester was prepared by reacting equimolar quantities of potassium p-nitrophenolate and methyl 2-bromopropanoate.

Thin-layer chromatography, used to check the purity of the product, showed two spots; one each from p-nitrophenol, and from methyl 2-(p-nitrophenoxy)propanoate. Since fairly reasonable separation of the mixture was achieved by thin-layer chromatography, dry column chromatography was attempted; methylene chloride was the eluting solvent and silica gel was the adsorbent, duplicating the conditions used in the TLC. This method was abandonned, however, since a good separation was difficult to achieve.

The next method of purification attempted was vacuum distillation; this, too, failed because p-nitrophenol decomposed.

Separation of the product mixture was achieved by washing the solid product with water. This method worked well because the p-nitrophenol is soluble in water. This method was avoided in the beginning because of uncertainty as to the stability of the methyl 2-(p-nitrophenoxy)-propanoate.

The next difficulty encountered concerned the synthesis and purification of 2-(p-nitrophenoxy)propanoic acid. Equimolar quantities of 2-bromopropanoic acid and potassium p-nitrophenol were refluxed for two hours in acetonitrile. This method of synthesis was employed because it seemed probable that it would work, was simple in technique, and was not time-consuming. A literature technique by Perron and Minor[5] is given below for comparison:

1) an equimolar mixture of 2-bromopropanoic acid and aqueous sodium hydroxide was cooled in an ice-water bath to keep the temperature below 30
2) p-nitrophenol is added in 5N sodium hydroxide
3) the mixture is heated on a steam bath for twenty hours
4) the mixture is cooled and then acidified to pH 2 with concentrated hydrochloric acid
5) the mixture is then extracted with ether
6) the ethereal solution is then extracted with 5% aqueous sodium bicarbonate
7) then the extracts are acidified after removal of the ether

This literature procedure was not attempted because a literature yield of only 21% was attained.

The product mixture's purity was checked by thin-layer chromatography, using methylene chloride as the developing solvent and silica gel as the adsorbent. The TLC showed three spots: one each from p-nitrophenol, 2-bromopropanoic acid, and 2-(p-nitrophenoxy)propanoic acid.

The first attempt to purify this mixture employed high pressure liquid chromatography with a reverse phase SE-30 dimethylsiloxane column. The HPLC employed was a Varian model 5000 Liquid Chromatograph with a Tracor 970 Variable wavelength detector. After a variety of compositions of eluting solvents were tried, it was found that a 40% acetonitrile, 60% water solution separated the mixture the best. Aliquots of the HPLC separation were collected at 45 second intervals and were analyzed by ultraviolet spectroscopy. The three components of the mixture still eluted close enough together, however, to eliminate this procedure as a purification technique.

The separation technique used was that of Perron, Minor, et al.(steps 5,6,and 7 of the technique above).[5] With this purification, a yield of about 30% was obtained.

There were several problems that had to be worked out before the apparatus could become fully functional. One major difficulty that had to be solved was the operability of the combination glass-pH electrodes at a high temperature. As stated in the experimental, certain problems were inherent with these electrodes since they were immersed in 80° solutions. At this high temperature, the concentration of the potassium chloride increases inside the electrode. After the reaction, as the temperature of the solution cools down, the potassium chloride comes out of solution, often times clogging the ion junction. When this occurs, the electrode cannot function properly and gives an erroneous pH reading.

One solution[6] to this problem is to realize that, since crystals blocking the junction may be present at room temperature, then the electrode may only read a reliable pH at an elevated enough temperature which redissolves these crysta The reliability of the electrode can be checked by measuring the pH of a buffer solution at that high temperature.

Another possible method[6] to solve this problem, although only attempted once here, is to remove the saturated potassium chloride solution before the electrode solution cools and to put warm water in to dissolve any crystals that reform as the electrode cools. Once the electrode has cooled to room temperature, the saturated potassium chloride is put into the electrode again. With this method, the ion junction is, in theory, never allowed to be blocked. The former method was used because the latter procedure always seemed to present a chance of damaging the inner components of the electrode when removing and injecting saturated potassium chloride and water solutions.

A few problems occurred with the constant temperature water bath system. Since the water was being heated at 80° it evaporated quite quickly. The water level in the vessel would become so low that it would cause the heating motor to start to function improperly. This problem was solved by putting aluminum foil wrapped cardboard covers on the vessels to reduce the evaporation.

Another difficulty occurred while trying to keep the reaction vessel temperature at 80°. The temperature was controlled to about ±2°. If the reaction started at 80°, often the temperature would rise or fall a degree or two. This lack of precise control is due to the heating motor and system.

Since there would be little, if any, evaporation problem it was originally desired to use silicone oil in the constant temperature bath. However, the silicone's high viscosity created stirring problems and thus, an even temperature distribution was difficult to achieve. Also, it was believed, at this elevated temperature, that the copper tubing may have been reacting with something in the silicone oil. This was evidenced by a greenish color developing in the silicone oil bath.

It was important to have good mixing in the reaction vessel so that the electrode would measure the correct pH and also so the reaction would occur uniformly and could be duplicated. Magnetic stirring bars and motors were used to achieve a uniformly mixed solution. Care had to be taken to ensure that vortexing in the reaction vessel did not occur, since the solution would then not be mixed and an inaccurate pH would be measured. By using the right size stirring bar(in this case 2.5 cm) and using the electrode itself as a baffle, good mixing of the solution was achieved.

B: Method of Analyzing Results

Two mL aliquots of the reaction mixture were withdrawn at time intervals of 2,5,7,10,15,20,25,30,40, 50,60,75,and 90 minutes, acidified with 12N hydrochloric acid and cooled. Through the use of NMR spectroscopy, each aliquot was analyzed for relative amounts of 2-bromopropanoic acid and 2-hydroxypropanoic acid(or lactic acid). Doublets for the methyl groups of lactic acid and 2-bromopropanoic acid occur respectively at 1.2 ppm and 1.6 ppm(relative to TMS at 0.0 ppm.)

The relative concentrations of the reactant and product were determined as follows: the average heights of both the reactant's doublet and the product's doublet were measured and then the sum of the two were taken. The concentration of 2-bromopropanoic acid was determined by dividing its average peak height by the total peak height. The same technique could be used to determine lactic acid's relative concentration.

A plot of log [2-bromopropanoic acid] versus time was then made, producing a straight line whose slope is -2.303k, where k is the first order rate constant. Each run consisted of 2-bromopropanoic acid and sodium hydroxide solution. These runs have not been controlled for a set ionic strength. Salt effects should be considered since the system deals with a weak acid. With any weak acid, like 2-bromopropanoic acid, it is expected that the addition of a salt will increase the degree of ionization slightly. This is due to interionic attractions to the strong electrolyte ions, thus causing the activities of the weak acid's ions to decrease.[7]

There is conflicting evidence as to how great an influence this will have on kinetic runs. The work of Lane and Heine[8] checked the possibility of a salt effect on runs with sodium α-bromocaproate and showed the rate of bromide ion formation conformed to a first order law.

Studies done by Leska and Bartko[9] have shown that a secondary salt effect is present. As evidence, they submit plots of k at different ionic strengths versus the acidity functions Q(+) and Q(-). Studies by C.K. Ingold[1] have also shown a secondary salt effect.

C: Results

This project deals with the kinetics of hyrolysis of 2-bromopropanoic acid. The methods of determining the relative concentrations of 2-bromopropanoic acid and lactic acid and of determining the rate constants have already been discussed.

Table 1 shows the rate constants at 80° for the decomposition of 2-bromopropanoic acid run at a pH of 3.3. Where the rate constants do not agree, poor temperature control and difficulties with NMR analysis can be blamed for the discrepancies. The poor temperature control plays the more important role. As stated earlier, it was sometimes difficult to keep the reaction vessel temperature exactly at 80° . The reaction temperature may have started at 80° but ten minutes later the temperature might be 78° or 82° . Action was taken to return the reaction vessel temperature to 80° , but even with prompt action, some of the reaction will have taken place at the higher or lower temperature. This affects the rate constant and thereby, the correlation coefficient.

The problem with the NMR analysis of the data is much more minor than that of the temperature control. Sometimes the sidebands from the NMR would interfere with the first few and last aliquots analyzed. This occurs firstly because of poor stability in the instrument and because in the beginning the lactic acid peaks are small and at the end the 2-bromopropanoic acid peaks are small. These small peaks can be obscurred by the sidebands of the larger peaks. This problem can be solved by subtracting the sidebands, but the accuracy of the result will not be as good as if there were no sidebands present.

D: Theory Behind Results

The hydrolysis of 2-bromopropanoic acid is a nucleophilic substitution of the halogen for OH^-. In this substitution, a pair of electrons are transferred from the nucleophile to the substitution site. From the substitution site, electrons are then donated to the leaving group.

This reaction is an example of the "three atom problem", in which one bond is broken and one bond is formed.[1] Two mechanisms are available for this nucleophilic substitution to proceed by; which mechanism predominates depends upon the structure of the molecule, that is, what substituents are located at the site of substitution.

The two available mechanisms for nucleophilic substitution are 1) bimolecular substitution(S_N2) and 2) unimolecular substitution(S_N1). Bimolecular substitution is characterized by the breakage of one bond and the formation of another bond, all in one continuous process. It is dependent upon the presence of a nucleophile. Kinetically, most of these bimolecular substitutions are of the second order. The S_N2 mechanism for the replacement of Hal by OH^- can be represented by:

$$\text{Alk-Hal} + OH^- \longrightarrow \text{Alk-OH} + \text{Hal}^-$$

Unimolecular substitution is characterized by the breakage of a bond in one step and the formation of a bond in another,separate step. Usually, they are of the first order kinetically. It can be represented by:

$$\text{Alk-Hal} \rightarrow \text{Alk}^+ + \text{Hal}^-$$

$$\text{Alk}^+ + H_2O \longrightarrow \text{Alk-OH} + H^+$$

The structure of the molecule at the site of the substitution greatly affects the mechanism of substitution. Bimolecular substitution is favored when electron withdrawing groups are present. The electron withdrawing groups remove the electrons from the approach of the nucleophilic reagent, and thus, the nucleophile can approach more easily. Unimolecular substitutions are favored when electron-supplying groups are present. This occurs because the electron-supplying groups help in the dissociation of the Alk-Hal species. The dissociation is a necessary first step in an S_N1 mechanism.

The effect of alkyl, aryl, carboxyl, and carboxylate-ion groups upon mechanism will now be briefly discussed.

Alkyl- The mechanism of substitution of halogen for OR in a methyl halide is strictly bimolecular. However, as these hydrogens are replaced by alkyl groups, such as methyl, the mechanism will change from bimolecular to unimolecular. This occurs because electrons are more easily released by alkyls than by hydrogens; that is, alkyls are more electron-repelling than are hydrogens. This change in mechanism can be seen by comparing the mechanisms present in the series[1] CH_3Cl,CH_2MeCl,$CH(Me)_2Cl$, and $C(CH_3)_3Cl$. The first member of the series has bimolecular substitution as its mechanism. The second and third members of the series show increasing amounts of reaction by the unimolecular mechanism, and the t-butyl chloride reacts by unimolecular substitution only.

Aryl- As with the alkyls, the aryls promote the unimolecular substitution mechanism. The aryls promote the S_N1 mechanism more strongly than alkyls, however, because of the aryl's high polarizibility.

In the series[1] Alk= CH_3,CH_2Ph, $CHPh_2$,and CPh_3, one can see the progression from bimolecular to unimolecular substitution. For Alk= CH_2Ph, the two mechanisms operate about equally. With Alk= $CHPh_2$, the unimolecular mechanism dominates, as is true with Alk=CPh_3.

An interesting example to look at is Alk= CHMePh; it is somewhat in between $CHMe_2$ and $CHPh_2$. If the reaction is run in aqueous solvent, the unimolecular substitution dominates, whereas in dry, alcoholic solvents, both the unimolecular and bimolecular substitutions operate.

Carboxyl groups- These are of the form CO_2R, which includes esters, carboxylamides, and undissociated carboxylic acids. These groups are electron-attractors and promote bimolecular substitution. As evidence of the promotion of bimolecular substitution, consider the species[1] Alk=$CHMeCO_2R$. If this was a simple, secondary alkyl halide it would have a unimolecular substitution mechanism. This species has bimolecular substitution, however.

Carboxylate-ion groups- This group also, like alkyls, repels electrons and thus as the carboxylate ion character begins to dominate the molecule, the mechanism will change from bimolecular to unimolecular substitution.

This can be seen in series [1] such as Alk= CH_3,CH_2CO_2-, $CH(CO_2)$- and Alk= CH_3,CH_2CO_2-, and $CHMeCO_2$-, where the mechanism progresses from S_N2 to S_N1.

Table 1: First Order Rate Constants for the Hydrolysis of 2-Bromopropanoic Acid at 80° ± 2° C at pH 3.3

k,min-1 (x10-3)	k,sec-1 (x 10-5)	Correlation Coefficient
3.56	5.93	0.9944
3.65	6.08	0.9820
3.81	6.35	0.9971
3.92	6.53	0.9916
4.32	7.20	0.9654
4.43	7.38	0.9893
4.64	7.73	0.9882
4.83	8.05	0.9909
4.87	8.12	0.9835
4.89	8.15	0.9877
4.95	8.25	0.9802
5.82	9.70	0.9386
6.05	10.1	0.9912
6.68	11.1	0.9810

Average k= 4.74x10-3 min-1

E: Discussion of Results and a Comparison to Literature Values

All of the experimental runs in Table 1 were run at a constant pH of 3.3. Even in an acidic solution, it is difficult to completely isolate the hydrolysis of the undissociated acid. The α-bromopropionate anion undergoes hydrolysis much more rapidly than does the undisociated acid. Even with the acid concentration much greater than the anion concentration, hydrolysis of the anion will occur.[1] It may be assumed, however, that the principal reaction will be the hydrolysis of the undissociated acid, although the anion hydrolyzes simultaneously.

Table 2, page 25, lists various literature values of the decomposition of 2-bromopropanoic acid. Each value is dependent upon temperature, pH, and ionic strength.

Table 3 lists the same literature sources with their rate constants corrected to a temperature of 80°C. The correction factor used was the rough rule of thumb of doubling the rate constant for every 10°C increase in temperature. Also listed in the table are the ionic strength of the reaction and the pH of the reaction.

The ionic strengths and pH values listed in Table 3 are the same as those in Table 2. Of course the pH changes as the temperature changes; these changes will not be that large over a temperature range of 20° or 30° C.

Table 2: Various Literature Values for the Decomposition of 2-Bromopropanoic Acid

Study	k1,min-1	Temp.	pH	Ionic Strength
Heine[10]	2.5x10-5	25	2.8	---
Heine[10]	4.25x10-3	59.75	2.8	---
Heine[10]	1.56x10-2	69.40	2.8	---
Ingold[1]	5.46x10-3	100	0.60	---
Leska[9]	6.6x10-3	90	2	---
Leska[9]	5.4x10-3	90	2	0.01
Leska9	1.86x10-2	90	2	2
Leska[9]	1.8 x10-3	90	0.3	0.5
Leska[9]	8.4 x10-3	90	0.3	2
Jensen	4.74x10-3	80	3.3	---

Table 3: Literature Values Corrected to 80°C;
A Comparison of this Work's k

Study	k1,min-1	pH	Ionic Strength
Heine	1.7x10-2	---	---
Heine	3.12x10-2	---	---
Ingold	1.37x10-3	0.60	---
Leska	3.3x10-3	2	---
Leska	2.7x10-3	2	0.01
Leska	9.3x10-3	2	2
Leska	9.0x10-4	0.3	0.5
Leska	4.2x10-3	0.3	2

A comparison will now be made between my experimental rate constant and literature values; discrepancies between the two will be explained. Comparing my rate constant at a pH of 3.3 to the value of C.K. Ingold, (pH 0.6) it is seen that my value is higher by a factor of about 3.5. This is because at the higher pH, the concentration of the anion is greater; since the hydrolysis of the anion occurs more rapidly, it is reasonable that my rate constant is higher than that of Ingold's.

Comparing my value to those of Heine's, my value is lower by factors of 3.6 and 6.6, respectively. Heine's reactions were run at a pH of 2.8. Thus, it is reasonable that his rate constants are higher than mine. Also, his reactions were not run at a constant pH and thus, his concentrations of acid and anion will change throughout the entire kinetic run.

Comparing my k to the second and third values of Leska, it is seen that my value of 4.74x10-3 is in between the values of 2.7x10-3 and 9.3x10-3. It seems reasonable that my kinetic runs had an ionic strength between 0.01 and 2. Once again, some of his runs were not run at a constant pH.

The mechanism of hydrolysis of undissociated 2-bromopropanoic acid is not demonstratable from the kinetics alone.[1] The slow rate suggests that it was bimolecular substitution. Studies[1] done on the optically active 2-bromopropanoic acid show that inversion occurs with no detectable racemization. Thus, this confirms the hydrolysis of the undissociated acid is bimolecular, though it is kinetically of the first order.

THE NEXT STEP

In the future, it is hoped to investigate the kinetics of hydrolysis of the α-bromopropionate ion using the pH stat system. The results will be analyzed by NMR spectroscopy. As the pH of the system rises, the bromoacid will become more dissociated and the anion concentration will be higher than that of the undissociated acid concentration. This, of course, changes the kinetics of the reaction. It has been shown[1] that at a low pH, the kinetics are of the first order. At higher pH's, both the first and second order kinetics proceed, depending upon the concentration of base. It is hoped that by changing the concentration of the base, both the first and second order processes will be isolated.

Another future goal is to investigate further the hydrolysis of methyl 2-bromopropanoate using alkaline and/or acidic solutions.[1] With an alkaline solution, the reaction has been shown to be of the second order kinetically, with a bimolecular mechanism; with acidic solutions, the reaction is of the first order, with a bimolecular substitution mechanism.[1] Studies done at 80° C and a pH of 4.0 have shown the methyl ester to be fairly unreactive.[11]

The methoxylation of the bromoester with sodium methoxide is fairly rapid and indicates second order.[1] Optical studies[1] have shown it to be of a bimolecular mechanism.

The acid methanolysis of methyl 2-bromopropanoate is slow;[1] hence, the reaction could be followed by NMR spectroscopy. Before this reaction starts, the solution will be neutral; it becomes acidic, however, since hydrobromic acid will be produced.

It is also desired to study the kinetics of 2-(p-nitrophenoxy)propanoic acid and methyl 2-(p-nitrophenoxy)propanoate. For both these compounds, it will be interesting to determine the effects of inductance and steric hindrance upon the kinetics. For the ester and the undissociated acid, the carboxyl groups are electron attractors and will promote bimolecular substitution. The big, bulky p-nitrophenoxy group, however, will cause steric hindrance problems, and would promote a unimolecular mechanism.

With the anion of the acid, the carboxylate-ion group will tend to repel electrons, and tend to promote unimolecular substitution. Sterically, the large group will promote S_N1.

CONCLUSION

Thus, it is easily shown that kinetics can be very dependent upon reaction conditions. In addition, it has been shown that inductance and steric effects play a major role in determining mechanisms of reactions. These studies have been of importance in determining general laws of mechanisms.

Thus, it has been shown that the kinetics of hydrolysis of α-bromopropionic acid can be investigated by use of an inexpensive pH stat system. The use of the pH stat system ensures that the pH will remain constant throughout the reaction. It was already stated that the works of Heine and Ingold were not controlled for pH, and thus were not as accurate.

This experimental work could be used as a physical chemistry project. Two options would be possible: either the students could do the experimental work themselves or be given the data to analyze. With the exception of the pH stat system, all of the equipment is common lab equipment.

Thus, this project could serve as an example of the dependence of mechanism and kinetics upon reaction conditions.

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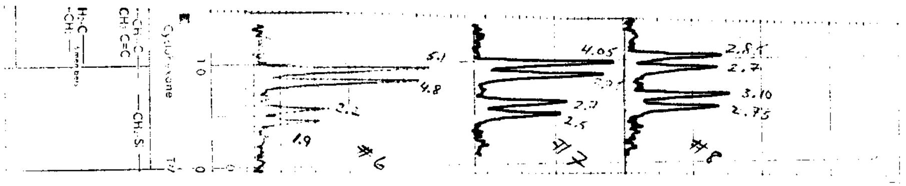
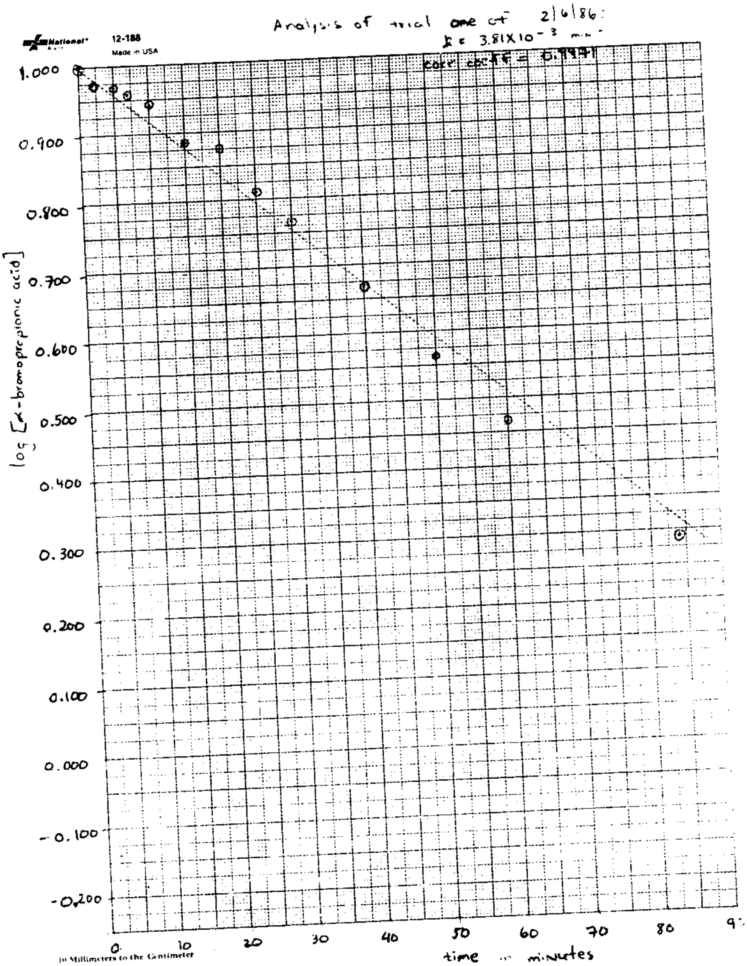
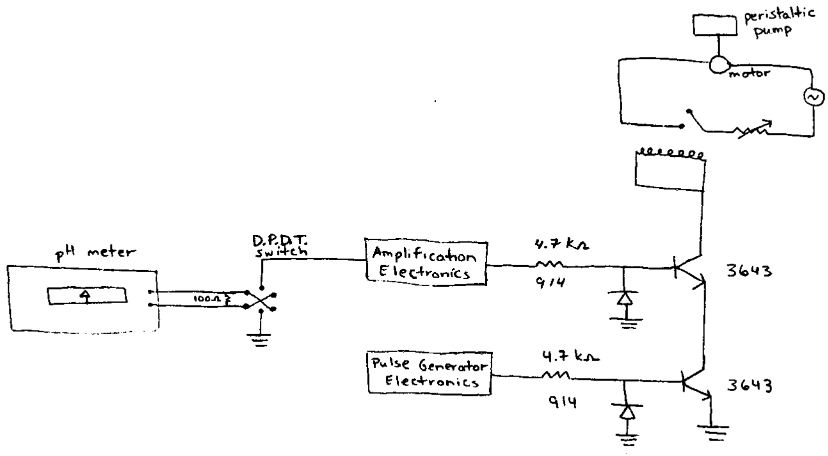
Appendix One: NMR's of a Kinetic Run of the Hydrolysis of 2-Bromopropanoic Acid at pH 3.3

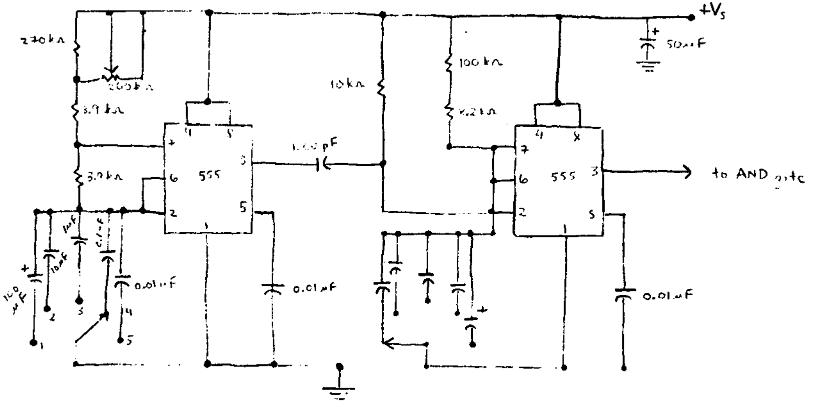




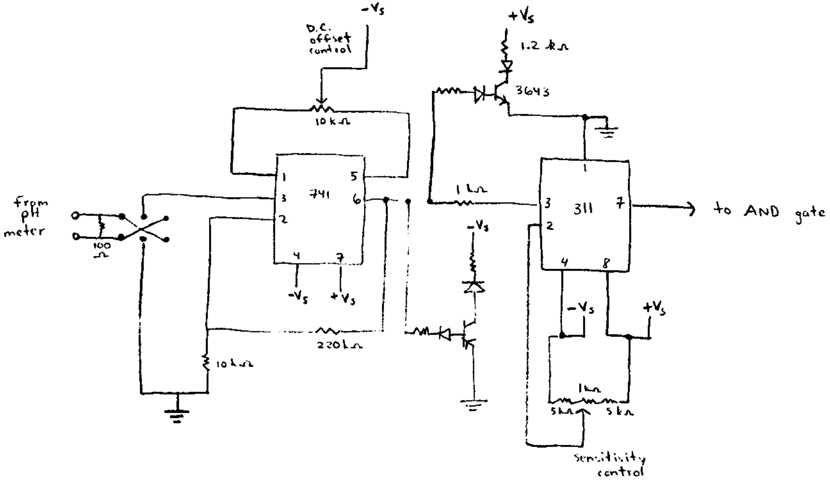
Appendix Two: Graph of Kinetic Data: Plots of log [2-Bromopropanoic Acid] v. Time



Appendix Three: Electronic Diagrams of pH Stat System

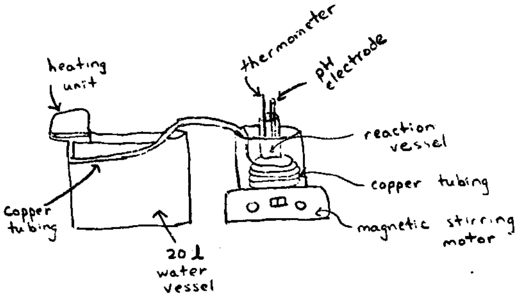


Appendix Three: Electronic Diagrams of pH Stat System



Appendix Three: Electronic Diagrams of pH Stat System

Reaction Vessel and Constant Temperature Bath



Appendix Four: Diagram of Experimental Apparatus