

# New insight on an old reaction – the aqueous hydrolysis of acetic anhydride

Floyd Landis Wiseman<sup>a,b,\*</sup>

Studies have shown that aqueous reactions generating a change in pH can be accurately monitored using a fast-response pH electrode. This technique has been successfully applied in this work to the aqueous hydrolysis of acetic anhydride, which is a reaction that has been studied using a variety of techniques for nearly one hundred years. Many of these techniques involve elaborate equipment and sophisticated analyses, making the pH technique an attractive alternative. Studies here have focused on the temperature effects of the simple hydrolysis and acetate-catalyzed hydrolysis reactions. Data analyses suggest the notion that if simple hydrolysis occurs by a two-step mechanism, it does so only at low temperatures, whereas acetate-catalyzed hydrolysis occurs almost assuredly by a single step mechanism. Results of this work yield the following values for the activation parameters for simple hydrolysis (subscripted with a “w”) and acetate-catalyzed hydrolysis (subscripted with an “a”) at atmospheric pressure:  $\Delta H_{\text{w}}^{\ddagger} = 39.9(0.7)\text{kJ}\cdot\text{mol}^{-1}$ ,  $\Delta S_{\text{w}}^{\ddagger} = -227(2)\text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$ ,  $\Delta H_{\text{a}}^{\ddagger} = 49.7(0.3)\text{kJ}\cdot\text{mol}^{-1}$  and  $\Delta S_{\text{a}}^{\ddagger} = -157(1)\text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$ . Implications of these results are discussed in this article. Copyright © 2012 John Wiley & Sons, Ltd.

**Keywords:** Acetic anhydride; Aqueous hydrolysis; General base catalysis; Eyring plot; Activation parameters

## INTRODUCTION

It seemed beneficial to apply the pH technique to a well-studied reaction such as the aqueous hydrolysis of acetic anhydride to make comparisons with the ample literature data. Hirota, Rodrigues, Sayer, and do Giudici<sup>[1]</sup> provide a brief history of the many studies conducted on this reaction. This list includes, but is not limited to, studies using titration,<sup>[2,3]</sup> calorimetric,<sup>[4–7]</sup> conductimetric,<sup>[8,9]</sup> spectroscopic,<sup>[10,11]</sup> temperature scanning,<sup>[12]</sup> and combination<sup>[13,14]</sup> techniques. The reader is referred to their article for more details. The pH technique, which has been successfully applied to the hydrolysis of the benzenediazonium ion,<sup>[15]</sup> entails the use of a pH meter to monitor aqueous reactions that undergo a pH change. This technique is particularly attractive since it does not require disturbing the reaction mixture, or involve elaborate experimental methods or complicated data analyses.

This work aptly demonstrates that the pH technique yields concise rate data for the aqueous hydrolysis of acetic anhydride. Non-linear regression analyses of the data (as pH vs. time) using the rate equations derived in this work yield correlation coefficients that are 0.99995 or better, and the correlation coefficients for the Eyring plots are on the order of 0.9999 or better.

This work presents separate analyses for simple hydrolysis and acetate-catalyzed hydrolysis. The acetate-catalyzed rate constants are about two orders of magnitude larger than the simple hydrolysis rate constants over the temperature range studied, large enough to make acetate-catalyzed hydrolysis significant even at fairly low acetate concentrations. These results are consistent with those of Butler and Gold.<sup>[16]</sup>

The literature on the hydrolysis of acetic anhydride has been littered with inconsistencies, as well as sketchy explanations for some of the results. For example, Robertson, Rossall, and Redmond<sup>[17]</sup> cite a value of  $-310\text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$  for the constant-pressure activation heat capacity ( $\Delta C_{\text{p}}^{\ddagger}$ ), but come to no concise

conclusion as to what this implies mechanistically. Literature results generally seem to indicate that the activation energy increases with the acetic acid concentration, but results are sometimes conflicting.<sup>[18]</sup> Hirota, Rodrigues, Sayer, and do Giudici<sup>[1]</sup> state that the activation energy apparently increases with the initial acetic anhydride concentration, but give no explanation for this trend.

Rather than focusing on mechanistic aspects, more recent articles discuss using acetic anhydride hydrolysis as a benchmark reaction for testing new or modified laboratory techniques. Rate constants and activation parameters generated from these studies are then compared with the prolific literature data. Unfortunately, the Arrhenius plots from most of the more recent work show some degree of data scatter,<sup>[9,12]</sup> making detailed comparisons tenuous. The data in this work, on the other hand, exhibits very little scatter.

Single-step and two-step steady-state mechanisms have been tested in this work. The general rate constant expressions from these mechanisms have been coupled with the Eyring equation to generate the temperature-dependent expressions for the rate constants. The data are analyzed using these expressions to generate a set of activation parameters for each of these mechanisms. The implications of these results are briefly discussed in light of the conventional understanding of the mechanism.

\* Correspondence to: Floyd Landis Wiseman, Chemistry & Physics, Coastal Carolina University, Smith Science Building, Conway, South Carolina 29528, United States. E-mail: fwiseman@coastal.edu

a F. L. Wiseman  
Chemistry & Physics, Coastal Carolina University, Smith Science Building, Conway, South Carolina 29528, United States

b F. L. Wiseman  
Home, 1740 Curlew Court, Viera, Florida 32955, United States

## THEORY

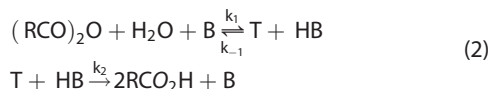
## The mechanisms

The reaction for the single-step mechanism is:



in which  $k_s$  is the single-step termolecular rate constant and B is either a second water molecule (simple hydrolysis) or another weak base (general base catalysis). In effect, B facilitates the attack of a water molecule at one of the carbonyl centers.

The two-step steady-state mechanism is<sup>[19,20]</sup>:



in which T is a tetrahedral intermediate. It is generally thought that more than two water molecules are involved in the rate-determining step.<sup>[21,22]</sup> However, since a two-water transition structure is sufficient to explain the data for phthalic anhydride hydrolysis,<sup>[23,24]</sup> the first step in Reaction (2) is treated here as termolecular. General nucleophilic catalysis is not an issue because the catalytic reactions were all executed with acetate buffers. Even though results from this work may have broader implications, discussions are limited to acetic anhydride hydrolysis where B represents either the acetate ion or another water molecule.

## The general rate law

For either mechanism, the rate law is first order provided the acetate ion concentration remains constant, i.e.:

$$[(\text{RCO})_2\text{O}] = [(\text{RCO})_2\text{O}]_0 e^{-kt} \quad (3)$$

in which  $[(\text{RCO})_2\text{O}]_0$  is the initial concentration and  $k$  is the experimental pseudo first-order rate constant. As will be demonstrated,  $k$  can be expressed in terms of the third-order rate constants,  $k_w$  and  $k_a$ , as:

$$k = k_w[\text{H}_2\text{O}]^2 + k_a[\text{H}_2\text{O}][\text{CH}_3\text{CO}_2^-] \quad (4)$$

The form of this equation actually used in this work is:

$$k = k'_w + \phi k'_a \quad (5)$$

in which  $\phi = \frac{[\text{CH}_3\text{CO}_2^-]}{[\text{H}_2\text{O}]}$ ,  $k'_w = k_w[\text{H}_2\text{O}]^2$ , and  $k'_a = k_a[\text{H}_2\text{O}]^2$ .

Table 1 shows the rate constant expressions for the single-step/two-step mechanism pairs. Derivations of these expressions are not shown since they can be derived by standard methods.

## The rate law in terms of the pH for a non-buffered solution

Use of the pH technique requires that Eqn (3) be recast in terms of the pH. However, the pH form of Eqn (3) is different for a buffered and a non-buffered system. The analysis for a non-buffered solution is as follows.

The hydrolysis of an anhydride leads to the formation of a weak acid, for which the equilibrium constant expression is:

$$K_{\text{acid}} = \frac{a_- a_+}{a} \quad (6)$$

in which  $a_-$  and  $a_+$  are the activities of the conjugate base and hydronium ion, respectively, and  $a$  is the activity of the undissociated acid. Noting that  $a_- = a_+$ , and  $a = \gamma \left( [\text{RCO}_2\text{H}] - \frac{a_+}{\gamma_+} \right)$ , in which  $\gamma$  and  $\gamma_+$  are the activity coefficients for the undissociated acid and hydronium ion, respectively, Eqn (6) becomes:

$$K_{\text{acid}} = \frac{a_+^2}{\gamma \left( [\text{RCO}_2\text{H}] - \frac{a_+}{\gamma_+} \right)} \quad (7)$$

Since  $[\text{RCO}_2\text{H}]$  is time varying, Eqn (7) is valid only if acid dissociation is fast relative to hydrolysis. Solving Eqn (7) for  $a_+$  yields:

$$a_+ = \frac{\gamma K_{\text{acid}}}{2\gamma_+} \left( \sqrt{1 + \frac{4\gamma_+^2 [\text{RCO}_2\text{H}]}{\gamma K_{\text{acid}}}} - 1 \right) \quad (8)$$

The acid and anhydride concentrations are related according to the following mass balance equation:

$$[\text{RCO}_2\text{H}] = [\text{RCO}_2\text{H}]_0 + 2 \left\{ [(\text{RCO})_2\text{O}]_0 - [(\text{RCO})_2\text{O}] \right\} \quad (9)$$

Noting that  $[(\text{RCO})_2\text{O}]_\infty = 0$ , Eqn (9) reduces to:

$$[\text{RCO}_2\text{H}] = [\text{RCO}_2\text{H}]_\infty - 2 [(\text{RCO})_2\text{O}] \quad (10)$$

Combining Eqns (3), (8), and (10) yields:

$$a_+ = \frac{\gamma K_{\text{acid}}}{2\gamma_+} \left\{ \sqrt{1 + \frac{4\gamma_+^2 [\text{RCO}_2\text{H}]_\infty}{\gamma K_{\text{acid}}} \left( 1 - \frac{2 [(\text{RCO})_2\text{O}]_0 e^{-kt}}{[\text{RCO}_2\text{H}]_\infty} \right)} - 1 \right\} \quad (11)$$

Finally, using the definition of pH (i.e.  $\text{pH} = -\log(a_+)$ ), Eqn (11) becomes:

**Table 1.** Combined rate constant expressions for the single-step and two-step steady-state mechanisms (Reactions (1) and (2))

Pathway pair	Equation designation	Expression for the experimental rate constant (k)	Definition of terms
Single step (w)/single step (a)	T1	$(k_w + \phi k_a)[\text{H}_2\text{O}]^2$	$\phi = \frac{[\text{CH}_3\text{CO}_2^-]}{[\text{H}_2\text{O}]}$
Single step (w)/two step steady state (a)	T2	$\left( k_w + \frac{\phi k_{a1}}{1 + \phi \alpha_a} \right) [\text{H}_2\text{O}]^2$	$\alpha_a = \frac{k_{a-1}[\text{H}_2\text{O}]}{k_{a2}}$
Single step (a)/two step steady state (w)	T3	$\left( \frac{k_{w1}}{1 + \alpha_w} + \phi k_a \right) [\text{H}_2\text{O}]^2$	$\alpha_w = \frac{k_{w-1}[\text{H}_2\text{O}]}{k_{w2}}$
Two step steady state (w)/two step steady state (a)	T4	$\left( \frac{k_{w1}}{1 + \alpha_w} + \frac{\phi k_{a1}}{1 + \phi \alpha_a} \right) [\text{H}_2\text{O}]^2$	

$$\text{pH} = -\log \frac{\gamma K_{\text{acid}}}{2\gamma_+} - \log \left\{ \sqrt{1 + \frac{4\gamma_+^2 [\text{RCO}_2\text{H}]_{\infty}}{\gamma K_{\text{acid}}} \left(1 - \frac{2[(\text{RCO})_2\text{O}]_0 e^{-kt}}{[\text{RCO}_2\text{H}]_{\infty}}\right)} - 1 \right\} \quad (12)$$

The activity coefficients are presumably constant during hydrolysis since the solutions are maintained at constant ionic strength. Equation (12) is statistically treated as a four-parameter equation. The parameters are  $-\log \frac{\gamma K_{\text{acid}}}{2\gamma_+}$ ,  $\frac{4\gamma_+^2 [\text{RCO}_2\text{H}]_{\infty}}{\gamma K_{\text{acid}}}$ ,  $\frac{2[(\text{RCO})_2\text{O}]_0}{[\text{RCO}_2\text{H}]_{\infty}}$ , and  $k$ .

### The rate law in terms of the pH for a buffered solution

The Henderson-Hasselbalch equation, which applies to buffer solutions, is:

$$\text{pH} = \text{p}K_{\text{acid}} + \log \frac{a_-}{a_+} \quad (13)$$

Using Eqn (3) and the principles of mass balance, Eqn (13) rearranges to:

$$\text{pH} = \text{p}K_{\text{acid}} + \log \frac{a_-}{\gamma [\text{RCO}_2\text{H}]_{\infty}} - \log \left(1 - \frac{2[(\text{RCO})_2\text{O}]_0 e^{-kt}}{[\text{RCO}_2\text{H}]_{\infty}}\right) \quad (14)$$

Because the solution remains buffered throughout the reaction,  $a_-$  is essentially constant. Equation (14) is treated as a three-parameter equation. The parameters are  $\text{p}K_{\text{acid}} + \log \frac{a_-}{\gamma [\text{RCO}_2\text{H}]_{\infty}}$ ,  $\frac{2[(\text{RCO})_2\text{O}]_0}{[\text{RCO}_2\text{H}]_{\infty}}$ , and  $k$ .

### The elementary rate parameters

In order to analyze the temperature dependency, every elementary rate constant and equilibrium constant appearing in the rate constant expression must be cast in a form that contains the temperature-dependent terms. For the elementary rate constants, this entails use of the Eyring equation. The form of the equation used in this work is:

$$k = \frac{k_B T}{h} \frac{\prod_{i=1}^n \gamma_i}{\gamma^\ddagger} (M^{1-n}) e^{\left[ \frac{\Delta S_r^\ddagger - \frac{\Delta H_r^\ddagger}{T} + \Delta C_p^\ddagger \left( \ln \frac{T}{T_r} + \frac{T_r}{T} - 1 \right) \right] / R} \quad (15)$$

in which  $k_B$  is Boltzmann's constant,  $h$  is Planck's constant,  $n$  is the molecularity,  $M$  is molarity ( $\text{mol}\cdot\text{dm}^{-3}$ ), the product term is over the reactant activity coefficients represented by  $\gamma_i$ ,  $\gamma^\ddagger$  is the transition structure activity coefficient,  $R$  is the gas constant,  $\Delta H_r^\ddagger$  is the activation enthalpy,  $\Delta S_r^\ddagger$  is the activation entropy,  $\Delta C_p^\ddagger$  is the temperature-independent activation heat capacity, and the subscript " $r$ " denotes a reference temperature. For both reaction pathways, there is no net change in overall charge as the transition structure is formed (there may, however, be a separation of charge). Therefore,  $\frac{\prod_{i=1}^n \gamma_i}{\gamma^\ddagger}$  is probably close to 1, in which case it can be dropped from the equation without losing too much precision. The values for  $n$  are: 3 for  $k_3$  and  $k_{11}$ ; 2 for  $k_{-1}$ ; and 1 for  $k_2$ . The kinetic parameters  $\alpha_w$  and  $\alpha_a$  are ratios of elementary rate constants (see Table 1), and are given by the general expression:

$$\alpha = \left( \frac{[\text{H}_2\text{O}]}{M} \right) e^{\left[ \frac{\Delta H_r^\ddagger}{T} - \Delta \Delta S_r^\ddagger - \Delta \Delta C_p^\ddagger \left( \ln \frac{T}{T_r} + \frac{T_r}{T} - 1 \right) \right] / R} \quad (16)$$

in which  $\Delta \Delta H_r^\ddagger = \Delta H_{r,2}^\ddagger - \Delta H_{r,-1}^\ddagger$ ,  $\Delta \Delta S_r^\ddagger = \Delta S_{r,2}^\ddagger - \Delta S_{r,-1}^\ddagger$ , and  $\Delta \Delta C_p^\ddagger = \Delta C_{p,2}^\ddagger - \Delta C_{p,-1}^\ddagger$ . For this work  $T_r$  is 25.0 °C and  $[\text{H}_2\text{O}]$  is approximately  $55.0 \text{ mol}\cdot\text{dm}^{-3}$ .

### The overall rate constant expressions

Equations (T2) and (T4) can be immediately eliminated since, as will be shown,  $k$  is linearly dependent upon  $\phi$  as depicted by Eqn (5).

*Rate constant expressions for equation (T1) (single-step for both reaction pathways)*

The single-step mechanism consists of a simple rate constant, and the general form is given by Eqn (15). In logarithmic form, the rate constant expressions are:

$$\ln \frac{k'_w h}{k_B T} = \frac{\Delta S_{w1}^\ddagger}{R} - \frac{\Delta H_{w1}^\ddagger}{RT} + \frac{\Delta C_{p,w}^\ddagger}{R} \left( \ln \frac{T}{T_r} + \frac{T_r}{T} - 1 \right) + 2 \ln \left( \frac{[\text{H}_2\text{O}]}{M} \right) \quad (17)$$

$$\ln \frac{k'_a h}{k_B T} = \frac{\Delta S_{a1}^\ddagger}{R} - \frac{\Delta H_{a1}^\ddagger}{RT} + \frac{\Delta C_{p,a}^\ddagger}{R} \left( \ln \frac{T}{T_r} + \frac{T_r}{T} - 1 \right) + 2 \ln \left( \frac{[\text{H}_2\text{O}]}{M} \right) \quad (18)$$

The last term on the right-hand-side of either equation converts the rate constants to pseudo first order. A linear plot of  $\ln \frac{k'_h}{k_B T}$  vs.  $\frac{1}{T}$  implies that  $\Delta C_p^\ddagger$  is close to 0. However, it is important to note that the term,  $\ln \frac{T}{T_r} + \frac{T_r}{T} - 1$ , is relatively small even for moderate temperature ranges. Hence, the magnitude for  $\Delta C_p^\ddagger$  must be fairly large to generate any discernible curvature in the plot.

*Rate constant expressions for equation (T3) (single-step for acetate-catalyzed hydrolysis and two-step for simple hydrolysis)*

The expression for the single-step acetate-catalyzed pathway is the same as for Eqn (T1), and is given by Eqn (18). The expression for the two-step simple water hydrolysis pathway, excluding the activation heat capacity terms, is:

$$\ln \frac{k'_w h}{k_B T} = \frac{\Delta S_{w1}^\ddagger}{R} - \frac{\Delta H_{w1}^\ddagger}{RT} - \ln \left\{ 1 + \left( \frac{[\text{H}_2\text{O}]}{M} \right) e^{\left( \frac{\Delta \Delta H_r^\ddagger}{T} - \Delta \Delta S_r^\ddagger \right) / R} \right\} + 2 \ln \left( \frac{[\text{H}_2\text{O}]}{M} \right) \quad (19)$$

The subscript " $r$ " has been excluded for brevity, and the heat capacity terms have been excluded to reduce the number of parameters in the regression analysis.

## EXPERIMENTAL AND DATA ANALYSES

Acetic anhydride (Baker, A.C.S. reagent) was used as received. Reaction solutions were made using distilled water, sodium acetate, acetic acid, and sodium chloride to adjust the ionic strength.

Temperatures were maintained at  $\pm 0.1$  °C using a water bath and a thermostatted water circulator (Lauda Ecoline Staredition). Since the thermostat only heated the water, ice was used to maintain temperatures lower than room temperature. The water bath was placed on a magnetic stirrer to ensure thermal equilibrium of the reaction solution. The reaction time was monitored

manually using a wristwatch with a second hand, and the pH was monitored using an Orion Thermo Scientific pH meter set to read to 0.001 pH unit and equipped with an Orion Ross pH electrode. The electrode was periodically calibrated using standard pH 7.00 and 4.01 buffer solutions (Spectrum).

Table 2 shows the concentrations for each buffer solution, the values for  $\phi$ , and the number of drops of acetic anhydride for each reaction solution. The ionic strength was maintained at  $0.500 \text{ mol}\cdot\text{dm}^{-3}$  using sodium chloride, and all reaction solutions had a density of  $1.020 (0.002) \text{ g}\cdot\text{cm}^{-3}$ . For each experimental trial,  $\sim 100 \text{ ml}$  of the reaction solution was slowly and continuously stirred in a 150-ml Erlenmeyer flask. After addition of the last drop of acetic anhydride, the pH electrode was inserted into the solution and secured. Reaction monitoring began between 20 and 45 s after addition of the last drop to allow the acetic anhydride time to dissolve. Four trials were conducted for each reaction solution. For the buffered solutions, the pH was around 5.5 with a range of 0.35 to 0.45 during hydrolysis. For the non-buffered solution, the pH was around 4 with a range of 0.7 to 0.9. The number of data points ranged from 20 for the faster reactions at higher temperatures to 35 for the slower reactions at lower temperatures. There was no indication of acid catalysis at these pH levels.

The raw kinetic data (as pH vs. time) was analyzed using Eqn (12) for the non-buffered solutions and Eqn (14) for the buffered solution. All data points were weighted equally in the regression analyses. The correlation coefficients ranged from 0.99995 for the faster reactions to 0.99999 for the slower reactions. Figure 1 shows a typical data set (pH vs. time) with the regression curve.

The resultant data at each temperature was then analyzed using Eqn (5). Figure 2 shows a typical data set ( $k$  vs.  $\phi$ ) with the regression curve, and Table 3 shows values for a representative set of rate constants. Finally, the data sets for  $k'_w$  and  $k'_a$  were analyzed using Eqns (17) – (19) to obtain the activation parameters for the suite of mechanisms. It is noted here that the method of Clarke and Glew<sup>[25]</sup> gave no improvement in the quality of the regression analysis and no change in the numeric values for the activation parameters.

## RESULTS AND DISCUSSION

### Regression analyses

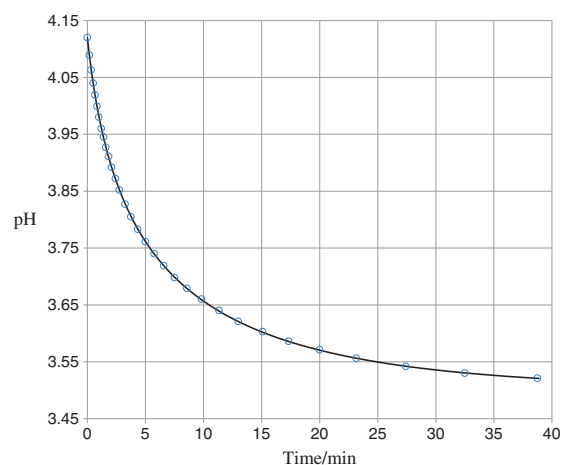
Figure 3 shows the plot of  $\ln \frac{k'_a h}{k_b T}$  vs.  $\frac{1}{T}$  with the regression analysis of Eqn (18), Fig. 4 shows the plot of  $\ln \frac{k'_w h}{k_b T}$  vs.  $\frac{1}{T}$  with the regression analysis of Eqn (19), and Table 4 shows the activation parameters from the regression analyses of Eqns (17) – (19).

**Table 2.** The buffer concentrations and values of  $\phi$  for each solution, and the number of drops of acetic anhydride. The acetic anhydride concentrations range from  $\sim 0.004 \text{ mol}\cdot\text{dm}^{-3}$  (1 drop) to  $\sim 0.06 \text{ mol}\cdot\text{dm}^{-3}$  (16 drops). The ionic strength is  $0.500 \text{ mol}\cdot\text{dm}^{-3}$  for all reaction solutions

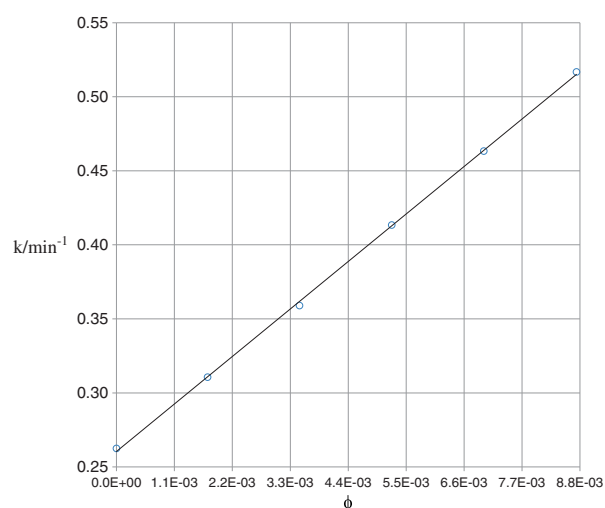
Initial acetic acid concentration/ $\text{mol}\cdot\text{dm}^{-3}$	Sodium acetate concentration/ $\text{mol}\cdot\text{dm}^{-3}$	Sodium chloride concentration/ $\text{mol}\cdot\text{dm}^{-3}$	$\phi$	Number of drops of acetic anhydride
0.000	0.000	0.500	0	1
0.0050	0.095	0.405	$1.730 \times 10^{-3}$	4
0.010	0.190	0.310	$3.477 \times 10^{-3}$	7
0.015	0.285	0.215	$5.229 \times 10^{-3}$	10
0.020	0.380	0.120	$6.976 \times 10^{-3}$	13
0.025	0.475	0.025	$8.735 \times 10^{-3}$	16

### Comparison with other work

The values for  $\Delta H_w^\ddagger$  ( $42.7$  and  $39.9 \text{ kJ}\cdot\text{mol}^{-1}$  from the analyses of Eqns (17) and (19), respectively) compare favorably with Robertson, Rossall, and Redmond's<sup>[17]</sup> value of  $40.2 \text{ kJ}\cdot\text{mol}^{-1}$ .



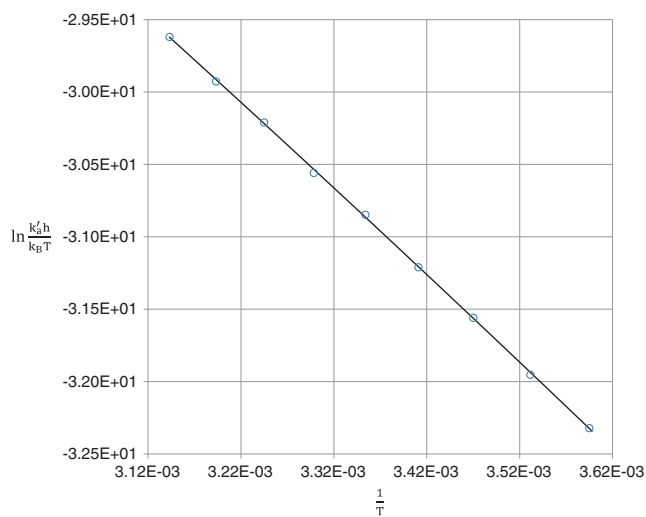
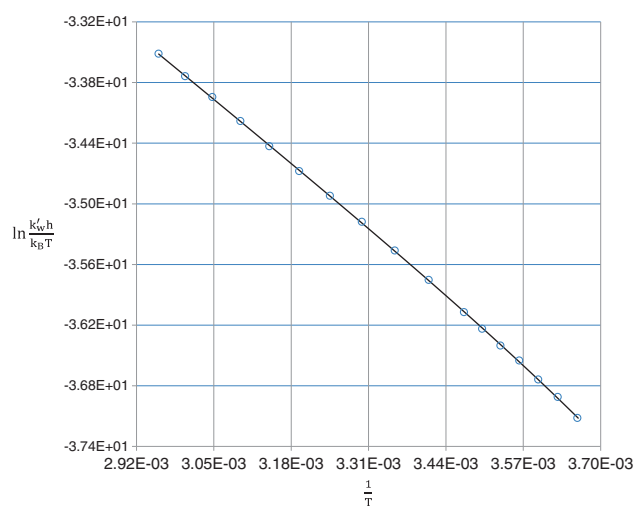
**Figure 1.** Typical kinetic data set showing the non-linear regression analysis of Eqn (12). Specifications:  $0.500 \text{ mol}\cdot\text{dm}^{-3}$  NaCl, non-buffered,  $12.5 \text{ }^\circ\text{C}$ ,  $k = 0.06492 \text{ min}^{-1}$ , correlation coefficient = 0.99999



**Figure 2.** Typical data set ( $k$  vs.  $\phi$ ) showing the linear regression analysis of Eqn (5). Specifications:  $35.0 \text{ }^\circ\text{C}$ ,  $k'_w = 0.260 \text{ min}^{-1}$ ,  $k'_a = 29.2 \text{ min}^{-1}$ , correlation coefficient = 0.9999

**Table 3.** Representative list of rate constants. Values for  $k'_w$  were obtained by regression analysis of Eqn (12) using the raw data (as pH vs. time for the non-buffered solutions). Values for  $k'_a$  were obtained by regression analysis of Eqn (5) using the data (as  $k$  vs.  $\phi$  for all solutions). The individual rate constants for the buffered solutions are not shown

Temperature/ $^{\circ}$ C	$k'_w/\text{min}^{-1}$	Percent of the standard deviation	$k'_a/\text{min}^{-1}$	Percent of the estimated error
0.0	0.02582	1.9		
2.5	0.03209	2.4		
5.0	0.03848	1.7	3.188	0.72
7.5	0.04682	1.6		
10.0	0.05481	1.1	4.694	0.92
12.5	0.06529	1.0		
15.0	0.07768	0.82	7.077	0.69
20.0	0.1086	1.0	10.20	0.81
25.0	0.1479	0.40	14.93	0.80
30.0	0.1998	0.32	20.25	0.15
35.0	0.2624	0.52	29.16	0.93
40.0	0.3407	1.0	39.36	0.89
45.0	0.4423	0.48	54.40	0.92
50.0	0.5751	0.46		
55.0	0.7427	0.69		
60.0	0.9262	1.4		
65.0	1.164	0.92		

**Figure 3.** Plot of  $\ln \frac{k'_w h}{k_B T}$  vs.  $\frac{1}{T}$  and the regression analysis of Eqn (18). The values from the analysis are  $\Delta H_a^\ddagger = 49.7$  (0.3)  $\text{kJ}\cdot\text{mol}^{-1}$ ,  $\Delta S_a^\ddagger = -157$  (1)  $\text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$ , and  $\Delta C_{p,a}^\ddagger = -67$  (50)  $\text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$ , and the correlation coefficient is 0.99990**Figure 4.** Plot of  $\ln \frac{k'_w h}{k_B T}$  vs.  $\frac{1}{T}$  and the regression analysis of Eqn (19). The values from the analysis are  $\Delta H_{w1}^\ddagger = 39.9$  (0.7)  $\text{kJ}\cdot\text{mol}^{-1}$ ,  $\Delta S_{w1}^\ddagger = -227$  (2)  $\text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$ ,  $\Delta \Delta H_w^\ddagger = 40$  (11)  $\text{kJ}\cdot\text{mol}^{-1}$ , and  $\Delta \Delta S_w^\ddagger = 191$  (42)  $\text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$ , and the correlation coefficient is 0.99998

The values for  $\Delta S_w^\ddagger$  ( $-218.3$  and  $-227 \text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$ ) are high compared with values from other work ( $-159 \text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$  from Robertson, Rossall, and Redmond<sup>[17]</sup> and  $-157$  to  $-189 \text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$  from Kokikallio, Pouli, and Whalley<sup>[26]</sup>). However, the values here are incrementally offset by  $-66.6 \text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$  due to the term  $2\ln[\text{H}_2\text{O}]$ , which does not appear in other work. The value for  $\Delta C_{p,w}^\ddagger$  ( $-106 \text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$ ) is significantly smaller than Robertson, Rossall, and Redmond's value of  $-310 \text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$ . However, the discussion in the following section sheds light on this disparity. To the author's knowledge, this is the only work addressing the activation parameters for the acetate-catalyzed hydrolysis.

### Mechanistic implications for simple water hydrolysis

Regression analyses of Eqns (17) and (19) are both good, with the latter being slightly better. Both models pass the F test, as noted in Table 4. Although this slight improvement is due in part to the fact that Eqn (19) is a four-parameter model, the difference in the functional behavior between Eqns (17) and (19) is probably a factor as well. Specifically, the activation heat capacity term contributes essentially uniform curvature in the Eyring plot, whereas the  $\alpha_w$  term in Eqn (19) (third term on the right-hand side) contributes regionally specific curvature. The experimental data exhibits some curvature at lower temperatures, and no discernible curvature above room temperature. Although this

**Table 4.** Results of non-linear regression analyses of the kinetic data. The entropic and heat capacity terms are in  $\text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$ , and the enthalpic terms are in  $\text{kJ}\cdot\text{mol}^{-1}$ . The estimated errors are shown in parentheses

Equations used in the analyses	Parameters and estimated errors from the regression analyses	Correlation coefficients	Pass F Test?
17	$\Delta S_{\text{w}}^{\ddagger} = -218.3(0.4)$ $\Delta H_{\text{w}}^{\ddagger} = 42.7(0.1)$ $\Delta C_{\text{p,w}}^{\ddagger} = -106(13)$	0.99996	Yes (for inclusion of $\Delta C_{\text{p,w}}^{\ddagger}$ term)
19	$\Delta S_{\text{w}1}^{\ddagger} = -227(2)$ $\Delta H_{\text{w}1}^{\ddagger} = 39.9(0.7)$ $\Delta\Delta H_{\text{w}}^{\ddagger} = 40(11)$ $\Delta\Delta S_{\text{w}}^{\ddagger} = 191(42)$	0.99998	Yes (for inclusion of $\Delta\Delta H_{\text{w}}^{\ddagger}$ and $\Delta\Delta S_{\text{w}}^{\ddagger}$ terms)
18	$\Delta S_{\text{a}}^{\ddagger} = -157(1)$ $\Delta H_{\text{a}}^{\ddagger} = 49.7(0.3)$ $\Delta C_{\text{p,a}}^{\ddagger} = -67(50)$	0.99990	No (for inclusion of $\Delta C_{\text{p,a}}^{\ddagger}$ term)

suggests that Eqn (19) better represents the results than Eqn (17), neither model can be definitively ruled out since both are statistically valid.

An estimate for  $\Delta C_{\text{p}}^{\ddagger}$  can be made from the following general equation:

$$\Delta C_{\text{p}}^{\ddagger} = 3(1 - n)R + \sum_{i=1}^{3N^{\ddagger}-6} C_{\text{p,vib,i}}^{\ddagger} - \sum_{j=1}^n \sum_{i=1}^{3N_j-6} C_{\text{p,vib,j,i}} + C_{\text{p,conf}}^{\ddagger} - C_{\text{p,conf}} \quad (20)$$

in which  $N^{\ddagger}$  is the number of atoms in the transition state,  $N_j$  is the number of atoms in species "j" of the reactant state,  $C_{\text{p,vib,i}}^{\ddagger}$  and  $C_{\text{p,vib,j,i}}$  are the expressions for the constant-pressure vibrational heat capacities, and  $C_{\text{p,conf}}^{\ddagger}$  and  $C_{\text{p,conf}}$  are the configurational terms associated with the intermolecular interactions. The first term on the right-hand side of the equation is the difference in the translational and rotational constant-pressure heat capacities in the high-temperature limit. This term is expected to make the largest contribution to  $\Delta C_{\text{p}}^{\ddagger}$ . With the possible exception of the few weak modes in the transition structure, the vibrational heat capacities terms are expected to make a somewhat smaller contribution. Unless significant differences exist in the solvent interactions between the reactant and transition states, the configurational terms are expected to make negligible contributions as well. With these assumptions, and noting that  $n=3$  for the forward step in Reaction (2), the estimated value for  $\Delta C_{\text{p}}^{\ddagger}$  is  $-6R$  ( $\sim -50 \text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$ ). A value on this order contributes only about 0.6% change in the value for  $\ln \frac{k_{\text{w,h}}}{k_{\text{s}}T}$  over the 65-degree temperature range in this work. This subtle effect is probably not discernible within the error estimates of the pH method, and is probably not discernible with most other methods. As a side note, the value of  $-106 \text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$  from the analysis of Eqn (17) suggests an involvement of five or six water molecules in the transition structure; whereas  $-310 \text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$  from Robertson, Rossall, and Redmond's work<sup>[17]</sup> suggests 13 or 14 water molecules!

The positive value for  $\Delta\Delta S_{\text{w}}^{\ddagger}$  indicates more structural constraints for the tetrahedral intermediate decomposing back to reactants than decomposing to products. This is plausible in light of the notion that a second water molecule may be facilitating the removal of the attached water molecule to reform the

reactants. The positive value for  $\Delta\Delta H_{\text{w}}^{\ddagger}$  indicates a somewhat larger energy demand for the intermediate decomposing to products. While this is difficult to visualize in terms of just bond rearrangements, it may suggest some degree of energy demand on solvent rearrangement to facilitate the acetate as a leaving group.

### Mechanistic implications for the acetate-catalyzed hydrolysis

The large estimated error for  $\Delta C_{\text{p,a}}^{\ddagger}$ , along with the failure of the F test for inclusion of the  $\Delta C_{\text{p,a}}^{\ddagger}$  term in Eqn (18), indicates this term is statistically insignificant and the Eyring plot is linear. However, it is worth noting that the value for  $\Delta C_{\text{p,a}}^{\ddagger}$  is close to  $-6R$ , suggesting the involvement of three molecules in the transition state, the least amount required for this reaction. It can further be concluded that the reaction does not involve the formation of a steady-state tetrahedral intermediate, at least not within the temperature range studied here. The values and estimated errors for  $\Delta H_{\text{a}}^{\ddagger}$  and  $\Delta S_{\text{a}}^{\ddagger}$  are the same in the regression analysis whether or not the  $\Delta C_{\text{p,a}}^{\ddagger}$  term is included.

### Contributions of this work

This work has aptly demonstrated the general viability of the pH technique for studying aqueous reactions that generate a pH change. It can be applied to buffered and non-buffered systems, and to reactions that generate or consume weak or strong acids or bases. The pH method has a further advantage in that it is easy to execute and does not involve lengthy sampling or extensive data analyses. Two drawbacks for this method are that it is not well suited for fast reactions (where  $k > \sim 1 \text{ min}^{-1}$ ) due to the limited response time of the electrode, and not suited for reactions in which the observed rate constant is pH dependent.

Probably the most important contribution of this work is the separate analyses for simple water hydrolysis and acetate-catalyzed hydrolysis. To the author's knowledge this is the first work to cite values for  $\Delta H_{\text{a}}^{\ddagger}$ ,  $\Delta S_{\text{a}}^{\ddagger}$  and  $\Delta C_{\text{p,a}}^{\ddagger}$ . Since  $k'_{\text{a}}$  is about two orders of magnitude larger than  $k'_{\text{w}}$ , an increase in acetate concentration as low as  $\sim 0.01 \text{ mol}\cdot\text{dm}^{-3}$  during hydrolysis will become autocatalytic. As a side note, Robertson, Rossall, and Redmond<sup>[16]</sup> conducted their kinetic experiments using

anhydride concentrations on the order of  $10^{-4}$  mol·dm<sup>-3</sup>, so catalysis is not an issue with their work. Since the importance of general base catalysis in ester and anhydride hydrolyses is common knowledge,<sup>[27,28]</sup> it seems odd that general base catalysis has not always been addressed where appropriate. Many of the anomalies and inconsistencies in the literature, particularly work involving higher concentrations of anhydride (e.g. Wilsdon, Sidgwick,<sup>[29]</sup> Asprey, Wojciechowski, Rice, and Dorcas,<sup>[12]</sup> and Haji, Erkey<sup>[11]</sup>) may be traced to a failure to account for this feature.

Finally, this work sheds some light on  $\alpha_w$ , which is the third term on the right-hand side of Eqn (19). Based upon oxygen-18 exchange studies in 60% dioxane/water, Bunton, Fuller, Perry, and Shiner<sup>[30]</sup> argued that  $\alpha_w$  should be 0.007 at 25 °C. On the other hand, Robertson, Rossall, and Redmond<sup>[17]</sup> argued that  $\alpha_w$  should be closer to 1 at 25 °C, in keeping with Bender and Heck's conclusion that  $\alpha_w$  is close to 1 for the hydrolysis of ethyl trifluoroacetate in 25% acetonitrile/water.<sup>[31]</sup> This work is more consistent with Bunton, Fuller, Perry, and Shiner's conclusion, and suggests that if intermediate tetrahedral formation is the correct mechanism, then  $\alpha_w$  is significant only at temperatures close to 0 °C (e.g.  $\alpha_w$  is 0.26 at 0 °C, but reduces to 0.06 at 25 °C).

#### Follow-on work

While Robertson, Rossall, and Redmond<sup>[16]</sup> measured the water/deuterium oxide kinetic solvent isotope effects for the water hydrolysis of acetic anhydride, studies need to be extended to determine the effects for the acetate-catalyzed hydrolysis. Proton inventory analyses for both reaction pathways would be beneficial for quantifying the number and types of protons involved in the transition structures. Robertson, Rossall, and Redmond<sup>[16]</sup> and Robertson and Rossall<sup>[22]</sup> also conducted extensive studies on the hydrolyses of other anhydrides, and estimated rather large negative activation heat capacities for some of these reactions. In light of the results from this work, the same type of studies presented here need to be extended to these other anhydrides to establish new baselines for these hydrolyses reactions.

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