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High information kinetic studies: non-isothermal programmed acid concentration kinetics

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Summary

The increasing availability of electronic equipment for automatic experiment control and data acquisition, and the availability of computing facilities make high information kinetic studies feasible. This latter phrase is used to describe kinetic experiments in which stability determining factors (e.g. pH, ionic strength, etc.,) are programmed within an experiment rather than several tests being performed each at a different level of the stability determining factor. Thus much more information can be extracted from a single experiment, and this should ultimately lead to decreased experimental effort.

This paper describes a non-isothermal, programmed acid concentration kinetic experiment through which the two rate constants and activation energies associated with the acid and solvent catalyzed hydrolysis of *p*-nitrophenyl acetate were simultaneously determined. Zero and infinite time assays were also estimated from the data. Results from this experiment were in close agreement with those from traditional (isothermal, fixed acid concentration) kinetic experiments and with estimates from non-isothermal fixed acid concentration tests.

The mathematical model developed for this situation accounts for volume change due to acid addition, sampling and thermal volume expansion. With minor modification it is applicable to other situations (e.g. ionic strength programming).

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Introduction

The phrase 'high information kinetic experiments' has been chosen to describe kinetic experiments in which a stability-determining factor (e.g. pH) is varied in a known way within an experiment. This can be compared with the traditional approach of conducting a number of experiments each at a different fixed level of the factor under consideration. The advantage of the new technique is that the effect of a factor or factors is determined from a single experiment and this has the potential to reduce experimental effort.

One currently used example of high information kinetic studies is the non-isothermal method (e.g. Edel and Baltzer, 1980) in which the temperature is programmed in a known way within an experiment enabling the frequency factor and activation energy to be estimated. However, other stability determining factors (e.g. pH, ionic strength, buffer concentration, etc.) might also be programmed but this has not been previously attempted.

The aim of this paper is to demonstrate the high information kinetic method using the hydrolysis of *p*-nitrophenyl acetate (PNPA) as a model reaction. PNPA is known to undergo acid, solvent, and base catalyzed hydrolysis (Connors, 1963) but below pH 3 the observed rate constant at any instant can be expressed as:

$$k = k_1 \cdot [H^+] + k_2 \cdot [H_2O] \qquad (1)$$

where k_1 and k_2 are the specific bimolecular rate constants associated with acid and solvent catalysis, respectively. But these two constants each have an associated activation energy (E_1 and E_2) so using the Arrhenius relationship:

$$k = k_{1a} \cdot e^{E_1/R \cdot (1/T_a - 1/T)} \cdot [H^+] + k_{2a} \cdot e^{E_2/R \cdot (1/T_a - 1/T)} \cdot [H_2O] \qquad (2)$$

where k_{1a} and k_{2a} are the bimolecular rate constants at temperature T_a, R is the Gas Constant, and T the absolute temperature.

Eriksen and Stelmach (1965) have stressed that use of the composite activation energy obtained from accelerated studies on a reaction of this type will lead to errors in the predicted shelf-life on the unsafe side and so have indicated a need to estimate the individual activation energies, E_1 and E_2. This usually requires multiple experiments at different pHs, each pH set being conducted at multiple temperatures. However, in this work, kinetic parameters (k_{1a}, k_{2a}, E_1 and E_2) were estimated from a single experiment in which both temperature and acid concentration were continuously varied.

Theoretical

If samples are withdrawn and cooled to the same analytical temperature (T_s) on each occasion, the molar concentration of reactant (C) at T_s equals m/V, where m is the moles of reactant and V the solution volume at T_s. Since both m and V are

functions of time (m due to reaction, V since acid is added continuously to the reaction vessel) then:

$$\frac{dC}{dt} = \frac{1}{V} \cdot \frac{dm}{dt} - \frac{m}{V^2} \cdot \frac{dV}{dt} \tag{3}$$

For a pseudo-first-order non-isochoric system (Livingstone, 1961):

$$-\frac{dm}{dt} = k_1 \cdot [H^+]' \cdot m + k_2 \cdot [H_2O]' \cdot m \tag{4}$$

where $[H^+]'$ and $[H_2O]'$ are the concentrations of these catalysts at any given instant. Since volume increases due to acid addition and thermal volume expansion, the instantaneous concentrations ($[H^+]'$ and $[H_2O]'$) are related to the instantaneous concentrations at T_s ($[H^+]$ and $[H_2O]$) by $f_2(t) = V/V'$ (i.e. the instantaneous volume at T_s divided by that at T) or $f_2(t) = V_{sp}/V'_{sp}$ (the specific volume of water at T_s divided by that at T). Thus Eqn. 4 becomes:

$$-\frac{dm}{dt} = (k_1 \cdot [H^+] \cdot m + k_2 \cdot [H_2O] \cdot m) \cdot f_2(t) \tag{5}$$

If acid is added at a constant rate ($\alpha l \cdot s^{-1}$ at T_s) and samples of volume V_s (at T_s) are withdrawn, analyzed then discarded, then the volume (at T_s) at any instant is:

$$V = V_0 + \alpha \cdot t - n \cdot V_s \tag{6}$$

where V_0 is the initial volume at T_s, and n the number of samples. Assuming samples are withdrawn instantaneously, then between samples:

$$\frac{dV}{dt} = \alpha \tag{7}$$

Substituting Eqns. 5 and 7 into Eqn. 3 yields:

$$\frac{dC}{dt} = (k_1 \cdot [H^+] \cdot C + k_2 \cdot [H_2O] \cdot C) \cdot f_2(t) + \frac{C \cdot \alpha}{V} \tag{8}$$

The reaction under consideration was followed spectrophotometrically so C was not known but only absorbance (A). Assuming that both reactant and product may absorb and both obey the Beer-Lambert Law and component absorbances are additive, then:

$$A = \epsilon_r \cdot b \cdot C + \epsilon_p \cdot b \cdot C_p + A_b \tag{9}$$

where ϵ_r and ϵ_p are the molar absorptivities of reactant and product, respectively, b the cell path-length, C_p the molar concentration of product, and A_b a constant background absorbance (zero-error). For the reaction under consideration we can

write $m_\tau = m + m_p$ (and $C_\tau = C + C_p$) where m is the number of moles of PNPA and m_p the number of moles of the product *p*-nitrophenol. Between any two samples m_τ is constant but since samples are discarded, m_τ between one pair of samples is different from that between another pair. Substituting the above equality into Eqn. 9 yields:

$$C = \frac{(A - A_b - \epsilon_p \cdot b \cdot C_\tau)}{(b \cdot (\epsilon_\tau - \epsilon_p))} \tag{10}$$

Now $C_\tau = m_\tau / V$ so:

$$\frac{dC_\tau}{dt} = \frac{1}{V} \cdot \frac{dm_\tau}{dt} - \frac{m_\tau}{V^2} \cdot \frac{dV}{dt} \tag{11}$$

But between samples m_τ is constant so:

$$\frac{dC_\tau}{dt} = -C_\tau \cdot \frac{\alpha}{V} \tag{12}$$

Substituting Eqn. 10 into Eqn. 8 and utilizing Eqn. 12 gives:

$$-\frac{dA}{dt} = \left\{ (k_1 \cdot [H^+] + k_2 \cdot [H_2O]) \cdot f_2(t) + \frac{\alpha}{V} \right\} \cdot (A - A_b)$$

$$- (k_1 \cdot [H^+] + k_2 \cdot [H_2O]) \cdot f_2(t) \cdot \frac{\epsilon_p \cdot b \cdot m_\tau}{V} \tag{13}$$

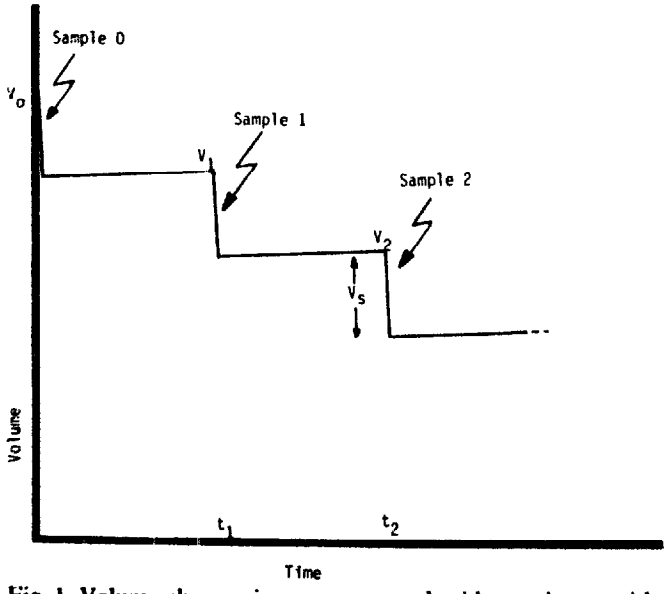

Fig. 1. Volume changes in a programmed acid experiment with sampling. Other abbreviations used: $m_{\tau 0}$, $m_{\tau s0}$, $m_{\tau 01}$, $m_{\tau 12}$ are total moles before sample 0, withdrawn in sample 0, and in the range sample 0–1 and 1–2, respectively; $C_{\tau 0}$ is the total concentration before sample 0; m_{H01}, m_{H12} are the moles of H^+ in the range sample 0–1 and 1–2, respectively; $M_0 = [H^+]$ at t=0; $M_B = [H^+]$ in the burette.

If the product does not absorb ($\epsilon_p = 0$), the second term on the right hand side, goes to zero and Eqn. 13 is analogous to Eqn. 8.

Variables requiring calculation are T, V, V′, m_τ and $[H^+]$. For non-isothermal kinetics, T is a function of time ($T = f_1(t)$) and this relationship is established from temperature–time data. V is calculated using Eqn. 6, and V′ from a knowledge of the thermal expansion coefficients of water. Using the nomenclature in Fig. 1, m_τ is determined as:

$$m_{\tau 01} = m_{\tau 0} - m_{\tau s0}$$

$$= m_{\tau 0} - C_{\tau 0} \cdot V_s$$

$$= m_{\tau 0} \cdot (1 - V_s/V_0)$$

$$= m_{\tau 0} \cdot f_0$$

Similarly

$$m_{\tau 12} = m_{\tau 01} \cdot (1 - V_s/V_1)$$

$$= m_{\tau 01} \cdot f_1$$

$$= m_{\tau 0} \cdot f_0 \cdot f_1 \qquad (14)$$

etc.

Thus $\epsilon_p \cdot b \cdot m_\tau$ (Eqn. 13) equals $\epsilon_p \cdot b \cdot m_{\tau 0} \cdot f_0 \cdot f_1 \ldots$ or $A_f \cdot f_0 \cdot f_1 \ldots$ where A_f represents the absorbance at infinite time if volume change had not occurred.

The moles of H^+ are calculated as:

$$m_{H01} = M_0 \cdot V_0 \cdot f_0 + \alpha \cdot t \cdot M_B$$

and

$$m_{H12} = M_0 \cdot V_0 \cdot f_0 \cdot f_1 + \alpha \cdot t_1 \cdot M_B \cdot f_1 + \alpha \cdot (t - t_1) \cdot M_B \qquad (15)$$

etc.

Thus $[H^+]$ can be determined from Eqns. 6 and 15.

Approximations (e.g. neglecting volume changes) could be made to simplify this mathematical model. Similarly experimental complexity could be increased to return samples after analysis. However, approximations will introduce unknown biases into parameter estimates while returning samples is not always applicable; for example, when destructive analyses are involved, or for spectrophotometric analyses which must be performed at constant temperature (T_s) because absorptivity is temperature dependent (Stearns, 1969). Since all computations are done by computer (where this mathematical model is easily handled) the philosophy has been to eliminate most approximations and keep the experimental system as simple as possible. The only simplification made is that samples are withdrawn instantaneously. This would seem

reasonable since the 15-s sampling time is small compared with the experimental time scale.

Materials and methods

Materials

PNPA was prepared by acetylation of *p*-nitrophenol (Fieser, 1941) and recrystallized to constant melting point (77.6°C) from fractionated benzene–petroleum ether (40–60°C) mixed solvent. *p*-Nitrophenol was recrystallized to constant melting point (115°C) from fractionated benzene and both materials were stored in vacuum desiccators in the dark until required. Differential thermal analysis showed the samples to be greater than 99.9% pure. Dilute acid (0.1045 M) prepared from concentrated hydrochloric acid (Baker Analysed Reagent) was standardized (Vogel, 1972) and further diluted as required. Burette acids were prepared from standard ampoules (Volucon) by dilution with glass distilled water. Reaction vessel acid was adjusted to the same ionic strength as the burette acid with sodium chloride (Ajax Chemicals A.R.).

Equipment

A one litre, closed stirred glass reaction vessel was immersed in a 60 litre P.E.G. 600 bath In isothermal experiments, temperature was controlled (±0.02°C) with a circulating heater (Gebruder Haake, Model ED Unitherm). A Gebruder Haake Temperature Programmer (PG12) was used for non-isothermal tests. Reaction vessel temperatures were monitored with a 4-lead platinum resistance thermometer (Degussa element, type P4) in conjunction with a Solartron Thermometer Unit (LU1962).

Concentrated acid was added automatically in increments of 0.01 ml from a Metrohm Hand Piston Burette (E274-20) fitted with a stepping motor drive (200 steps per rev.). Samples were withdrawn automatically and immediately quenched by cooling to 32°C in a water-jacketed teflon coil. The cooling time was less than 10 s. After cooling samples were automatically transferred to a 2 mm quartz flow-cell and analyzed spectrophotometrically (Perkin Elmer Model 124) 28 s after removal from the reaction vessel. The solution in the dead volume between the cooling coil and reaction vessel (approximately 1 ml) was returned to the reaction vessel 10 s after being withdrawn (Tucker, 1980).

Analysis

Absorbances were determined at 318 nm (Eriksen and Stelmach, 1965). Spectra from an isothermal fixed acid test showed a single isobestic point (292 nm) indicating a one-to-one reaction and stability of the absorbing product *p*-nitrophenol. The final spectrum was identical with that of *p*-nitrophenol.

A Beer-Lambert calibration in distilled water, using replicate samples, confirmed linear concentration absorbance relationships for PNPA and *p*-nitrophenol and that component absorbances were additive. Spectra in distilled water and acid were identical.

Kinetic procedure

One litre of acid was equilibrated thermally then about 80 mg of PNPA dissolved in 2 ml of fractionated ethanol was added and the temperature programmer started. The solution was bubbled with high purity nitrogen. The first sample was withdrawn 2 min later and the addition of concentrated acid started. At each sampling, reaction vessel temperature, sample absorbance, volume of acid added, and time were automatically recorded.

Design

Replicate isothermal tests were performed at the acid concentrations and temperatures shown in Table 1. About 30 data were collected during each experiment. For the non-isothermal variable acid tests, various approximately linear temperature and acid programmes were tried as well as a cycling temperature program. About 50 data were collected per run and the reaction was studied over at least 90% decomposition.

Computational procedures

Isothermal pseudo-first-order rate constants were estimated by non-linear least-squares regression (using Marquardt's 1963 algorithm) of absorbance on time, treating k, initial absorbance (A_0) and infinite time absorbance (A_∞) as parameters. The adequacy of the model was judged by the Runs Test (Draper and Smith, 1968) and by a comparison of the residual variance with the error variance of the experimental system known from a great deal of previous experience. Bimolecular rate constants at each temperature were estimated by linear regression and a variance ratio test was used to test the adequacy of the model. These rate constants were then used to estimate E_1 and E_2 by linear least-squares regression.

For non-isothermal data, temperature time relationships ($f_1(t)$) were established in 3 ways: for approximately linear temperature programmes an orthogonal polynomial

TABLE 1

OBSERVED PSEUDO FIRST-ORDER RATE CONSTANTS (10^4 s^{-1}) FOR THE ISOTHERMAL HYDROLYSIS OF PNPA

Temperature (°C)	Acid concentration (M)		
	0.01045	0.05223	0.1045
54.95	0.1251	0.3988	0.7344
	0.1250	0.3966	0.7384
	0.1252	0.4002	0.7422
69.42	0.3489	1.1901	2.2260
	0.3529		2.2253
	0.3485		
82.72	0.8364	3.0020	5.6293
	0.8478	2.9957	5.6589
	0.8526		

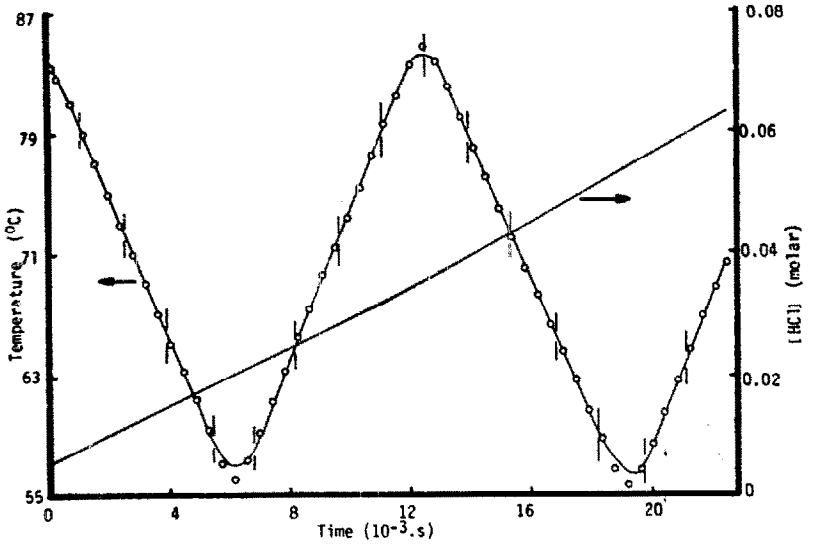

Fig. 2. Acid and temperature programmes for a non-isothermal programmed acid hydrolysis of PNPA. Vertical lines indicate the knot positions used in the cubic spline fit.

regression programme (Stewart, 1975) was used to determine the polynomial of lowest order which adequately described the data. However, this was unsuitable for the cycling programme (Fig. 2) hence a cubic spline programme (Powell, 1967) was used to determine a smooth least squares fit to the data. Thirdly, linear interpolation was employed to estimated temperatures between data points.

A polynomial was established for the specific volume of water versus temperature using literature data (Weast, 1974). This function in conjunction with $f_1(t)$ defines $f_2(t)$.

The non-linear regression programme was used to estimate k_{1a}, k_{2a}, E_1 and E_2, using the Arrhenius equation and Eqns. 6, 13, 14 and 15 together with $f_1(t)$ and $f_2(t)$. Initial estimates for this iterative procedure were obtained by a differential non-isothermal solution of the data (Anderson and Campbell, 1971). The differential equation (Eqn. 13) was solved using the Kutta-Merson method (Fox and Mayers, 1968). Starting values are required for this procedure (i.e. $A = A_0$ at $t = 0$) for the range from sample 0 to 1. A_0 was treated as a parameter so estimated from the data. New starting values are required for subsequent ranges and these were provided by the calculated A values at each sampling time. A_f was also treated as a parameter (thus 6 parameters in all) while A_b was determined from multiple measurements of the zero-error. Adequacy of the model was judged as for the isothermal data analysis.

The truncation error in calculated A values was a factor of 10 less than the random error in the data and hence did not contribute significantly to the sum of squares. Further decrease in this truncation error did not alter the parameter estimates but only increased computational time.

Results and discussion

Isothermal

The first-order model was found to describe the data adequately. Observed rate constants are shown in Table 1. Regressions of k-observed on $[H^+]$ at each temperature showed no significant curvature confirming that Eqn. 1 was an adequate model. Arrhenius plots for the bimolecular rate constants appeared linear, there being no replicates available to test for curvature. Kinetic parameter estimates and standard deviations were $E_1 = 17.16 \pm 0.024$, $E_2 = 14.29 \pm 0.159$ kcal $\cdot$ mol^{-1}, and for $T_a = 65°C$ $k_{1a} = 1.431 \pm 0.002 \times 10^{-3}$ l $\cdot$ mol^{-1} s^{-1} and $k_{2a} \cdot [H_2O] = 1.096 \pm 0.009 \times 10^{-5}$ s^{-1}. Because the error estimates from these regressions are based on one degree of freedom, the confidence limits of these parameters are quite wide (e.g. 95% C.L. on $E_1 = \pm 0.305$).

Function $f_2(t)$

A suitable polynomial relating specific volume of water (V'_{sp}) to temperature for the range 30–92°C was found to be

$$V'_{sp} = 0.99992806 - 0.35791641 \times 10^{-4} \cdot T + 0.72094751 \times 10^{-5} \cdot T^2 - 0.42243321 \times 10^{-7} \cdot T^3 + 0.21949816 \times 10^{-9} \cdot T^4 - 0.47002556 \times 10^{-12} \cdot T^5 \quad (16)$$

where T = °C for this equation. All residuals about this regression were less that 7×10^{-7} ml g^{-1} and randomly distributed. The function $f_2(t)$ where $T_s = 32°C$ is equal to:

$$f_2(t) = \frac{V_{sp}}{V'_{sp}} = \frac{1.004995}{V'_{sp}} \quad (17)$$

Function $f_1(t)$

For the approximately linear temperature programmes, polynomials of fourth order or less were found adequate. The residual mean square about these regressions was typically 0.01 corresponding to a standard deviation of a reading of ±0.1°C. Residuals about the regressions were randomly distributed.

For the temperature cycling programme shown in Fig. 2 a polynomial was not suitable. Even a ninth order polynomial had residuals as large as 2.2°C. This is due to the sharp turning points in the temperature programme. Consequently, alternative methods were used.

The cubic spline programme automatically divides the curves at knots (Fig. 2). Each interval is a segment of a cubic curve, and these are smoothly joined. Smoothly here means continuous function, first, and second derivatives and minimized discontinuity in the third derivative. The functional values and first derivative at the knots

were used in the non-linear regression programme to compute intersample temperatures.

Although the residuals about the cubic spline fit are random, the fit near the turning points is poor with a maximum residual of −1.09°C. This could be overcome by using a temperature programme with broader turning points. However, Madsen et al. (1974) have pointed out that the random fluctuations tend to average out during the non-linear regression.

The third method of computing intersample temperatures by linear interpolation is equivalent to joining the data points of Fig. 2 by straight lines. It implies that the temperatures are measured without error. Provided the random errors in this variable are small, this is a reasonable assumption and once again, errors tend to average out during the non-linear regression. A quadratic interpolation could have been used to minimize errors at the turning points; however, because data were available close to the peaks, this was unnecessary.

Programmed acid

Before conducting experiments in which both acid and temperature were varied, an experiment was performed in which acid concentration only was continuously varied. This was achieved by addition of approximately 1 M HCl (50 ml) giving an

TABLE 2

ISOTHERMAL HYDROLYSIS OF PNPA WITH PROGRAMMED ACID CONCENTRATION

Constant values:

Initial volume (V_0)	1.000 l
Sample volume (V_s)	0.00577 l
Initial acid conc. (M_0)	0.005223 M
Burette acid conc. (M_B)	0.9968 M (50 ml added)
Addition rate (α)	2.783×10^{-6} l·s^{-1}
Temperature (T)	82.72°C
Background (A_b)	1×10^{-3} A.U.

Parameter	(1)	(2)	(3)	(4)	(5)
$10^3\cdot k_1$ (l·mol^{-1} s^{-1})	5.146	5.115	5.176	5.143	5.148
$10^5\cdot$SE (k_1) [a]	2.3	–	–	–	–
$10^5\cdot k_2\cdot[H_2O]$ (s^{-1})	3.182	3.198	3.166	3.185	3.179
$10^7\cdot$SE ($k_2\cdot[H_2O]$) [a]	3.5	–	–	–	–
A_0 (A.U.)	0.1574	0.1574	0.1574	0.1574	0.1574
A_f (A.U.)	0.9670	0.9625	0.9715	0.9670	0.9665
$10^7\cdot$Error Var. (A.U.^{2}) [c]	2.82	2.85	2.80	2.85	2.80
Runs Prob. [b]	0.5	0.5	0.5	0.5	0.5
V_0 (l)	1.0	0.995	1.005	1.0	1.0
V_s (ml)	5.77	5.77	5.77	5.80	5.74

[a] Standard error of parameter shown; units as for the parameter.

[b] Probability from the Runs test for non-random residuals.

[c] Based on experience this value should be in the range 1×10^{-7} to 9×10^{-7} A.U.^{2}.

acid concentration range of 0.005–0.05 M. Addition was sufficiently slow so that no temperature change was detectable. Constant values used in this test are shown in Table 2. Also shown in column 1 of Table 2 are the least-square parameter estimates and the statistics (Error Var. and Runs Prob.) for judging the adequacy of the first-order model. The estimates are in good agreement with the isothermal values of $k_1 = 5.104 \times 10^{-3}\,l \cdot mol^{-1}\,s^{-1}$ and $k_2 \cdot [H_2O] = 3.160 \times 10^{-5}\,s^{-1}$ at this temperature. The coefficient of variation for k_1 is less than that for $k_2 \cdot [H_2O]$ since the solvent-catalyzed reaction makes a small contribution to the overall reaction for more than 95% of the experimental time.

The effect of errors in V_0 and V_s upon the parameter estimates was investigated. Columns 2 and 3 show the estimates when V_0 is varied by ± 5 ml, while columns 4 and 5 show the results when V_s was increased and decreased by 3 S.D.s of the mean sample volume. Changes caused by the shifts in V_s are very small. Those caused by incorrect V_0 values are greater but still lie within the 95% C.L. of the parameters. In any case, suitable procedures would limit the error in V_0 to much less than that tested. Thus the estimates are reasonably insensitive to errors in these constants. Addition rate was precisely known and so was not tested.

It is concluded that this isothermal procedure provides a rapid means of estimating bimolecular rate constants in acid/solvent-catalyzed reactions. It should also be applicable in alkaline regions.

Programmed acid and temperature

Tests were performed over a temperature range of 85–50°C with approximately linear temperature programmes of -3°C and -6°C/h. Initial reaction vessel acid concentrations of 0.005 and 0.01 M were used. Burette acid concentrations were 1 and 2 M HCl and 50 ml of this was added to a 1 litre reaction solution. Thus reaction vessel acid increased to either 0.06 or 0.12 M during experiments.

Based on the isothermal kinetic parameter estimates, the solvent-catalyzed reaction was making a significant contribution (about 50% decreasing to 5%) to the decomposition. However, all attempts to estimate kinetic parameters as well as A_0 and A_f failed. When A_0 and A_f were treated as known constants, the non-linear regression programme did converge on one occasion, but the confidence limits of the parameters were extremely wide (e.g. 95% C.L. for E_2: 10–49 kcal $\cdot$ mol^{-1}). This is clearly unacceptable. All correlation coefficients between parameters exceeded 0.98.

It was concluded that the lack of success in estimating parameters from these experiments was due to the high correlation between acid concentration and temperature (typically $r = -0.99$). In hindsight it is clear that when parameters associated with particular experimental variables are to be estimated simultaneously, the variables should be altered in such a way as to minimize correlation between them. Appropriate variable programmes could be determined by simulation studies thereby avoiding wasted experimental effort.

To eliminate this high correlation temperature was programmed up and down for several cycles while the same linear acid programme was maintained (Fig. 2). This reduced the correlation coefficient to $r = -0.3$. Although acid was added at a constant rate, the decreasing reaction solution volume (due to sampling) led to the

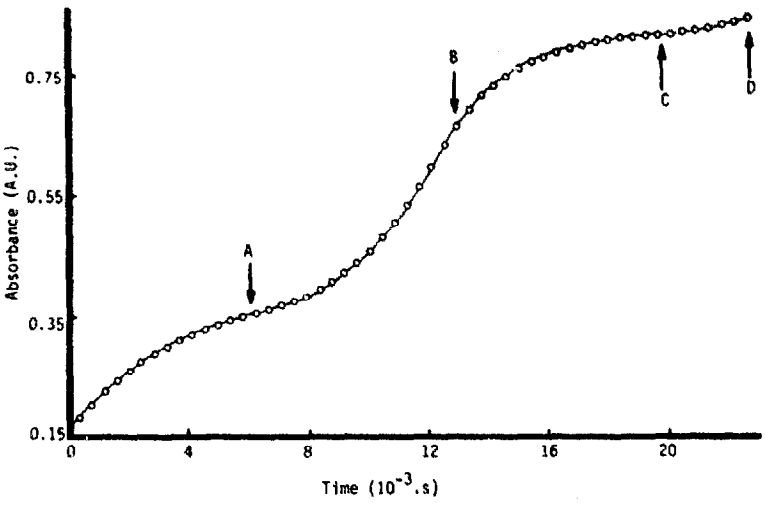

Fig. 3. Absorbance changes during a non-isothermal programmed acid hydrolysis of PNPA, and showing the least-squares regression line.

TABLE 3

NON-ISOTHERMAL HYDROLYSIS OF PNPA WITH PROGRAMMED ACID CONCENTRATION

Constant values:

Initial volume (V_0)	1.000 l
Sample volume (V_s)	0.00577 l
Initial acid conc. (M_0)	0.005223 M
Burette acid conc. (M_B)	0.9968 M (50 ml added)
Addition rate (α)	2.273×10^{-6} l·s^{-1}
Temperature range	Cyclic 56–85°C
Background (A_b)	5×10^{-4} A.U.

Parameter	Linear [d]	Spline [e]
$10^3\cdot k_{1a}$ (l·mol^{-1} s^{-1}) [f]	1.471	1.460
$10^5\cdot$SE (k_{1a}) [a]	1.9	2.1
$10^5\cdot k_{2a}\cdot[H_2O]$ (s^{-1}) [f]	1.088	1.111
$10^7\cdot$SE ($k_{2a}\cdot[H_2O]$) [a]	3.0	3.4
E_1 (kcal·mol^{-1})	17.08	17.14
10·SE (E_1) [a]	1.6	1.8
E_2 (kcal·mol^{-1})	14.04	13.60
10·SE (E_2) [a]	5.3	5.8
A_0 (A.U.)	0.1652	0.1654
A_f (A.U.)	1.0105	1.0115
10^7 Error Var. (A.U.^{2}) [c]	2.25	2.75
Runs Prob. [b]	0.5	0.5

[a, b, c] As for Table 2. [d] Temperatures calculated by linear interpolation or [e] cubic spline. [f] T_a 65°C.

upward curvature evident in the acid programme graph.

The resultant absorbance time data are shown in Fig. 3. The curve through the points is the least-squares regression line when cubic spline or linear interpolation temperatures were used.

The rate of reaction at any instant is determined by: acid concentration, temperature and reactant concentration. These effects are apparent in Fig. 3. From time zero to A and from B to C the rate decreases due mainly to the decreasing temperature and partly because PNPA is consumed. From A to B and C to D the rate increases due to increasing temperature. The rate of increase over C to D is less than that from A to B because the decreased PNPA concentration outweighs the increased acid concentration. Finally the rate around B exceeds that around time zero since the effect of increased acid outweighs the decreased PNPA concentration.

The least-square estimates and statistics for judging adequacy of the model are shown in Table 3. Results for the two methods of temperature calculation are not significantly different and the fits are adequate in both cases. Standard errors for k_{2a} and E_2 are greater than those for k_{1a} and E_1 (although all standard errors are acceptably small) since the solvent-catalyzed reaction made a smaller contribution to the overall reaction. This situation was also observed for the isothermal kinetics.

Comparison of methods

The kinetic parameter estimates are summarized in Table 4. Methods 5 and 6 of Table 4 are estimates in 0.2396 M HCl. At this concentration the solvent catalyzed pathway contributes less than 5% (percentage depends on T); therefore, the observed activation energy is approximately E_1.

Agreement among estimates is good. The ranges for k_{1a}, $k_{2a} \cdot [H_2O]$, E_1 and E_2 estimated in this laboratory are 3.1%, 3.7%, 1% and 4.9% respectively. These differences not only include within experiment variation but also between experiment factors such as different acid solutions. The range for E_2 is not unacceptable considering the contribution made by the solvent-catalyzed reaction. Its precision could be improved by working at lower acid concentrations but this would lead to longer experiments. Agreement with literature rate constant values is reasonable. The standard error for Eriksen and Stelmach's (1965) estimate of k_{1a} is $\pm 0.31 \times 10^{-3}$ which easily brackets the estimates determined by the authors. The standard error of Connors' (1963) estimate is not available.

There is some discrepancy between estimates of E_1. Eriksen and Stelmach's estimate of 21 ± 2 kcal $\cdot$ mol^{-1} seems a little high, although their 95% C.L. would take in the authors' estimates of E_1. Their isothermal estimate of 18 kcal $\cdot$ mol^{-1} is in reasonable agreement but confidence limits for this are not available.

Of most interest is a comparison between the traditional isothermal approach and the new method. In a statistical sense there is no difference between estimates determined in this laboratory since the 95–99% C.L. of the isothermal estimates bracket those from other methods. In a practical sense the estimates can be considered identical.

Other

The equations developed are also applicable to the programming of other stability

TABLE 4

KINETIC PARAMETER ESTIMATES DETERMINED BY VARIOUS METHODS FOR THE HYDROLYSIS OF PNPA

Method	$10^3 \cdot k_{1a}$ [a] ($l \cdot mol^{-1} s^{-1}$)	$10^5 \cdot k_{2a} \cdot [H_2O]$ [a] (s^{-1})	E_1 ($kcal \cdot mol^{-1}$)	E_2 ($kcal \cdot mol^{-1}$)
1 [b]	1.431	1.096	17.16	14.29
2 [c]	1.460	1.111	17.14	13.60
3 [d]	1.471	1.088	17.08	14.04
4 [e]	1.446	1.129	–	–
5 [f]	1.481 [k]	–	17.00	–
6 [g]	1.470 [k]	–	16.98	–
7 [h]	1.63	0.90	–	–
8 [i]	1.55	–	21	–
9 [j]	–	–	18	–

[a] $T_a = 65°C$; [b] isothermal; [c] non-isothermal programmed acid, spline method.

[d] As for c but linear method; [e] isothermal programmed acid, calculated using $E_1 = 17.13$, $E_2 = 13.98$ $kcal \cdot mol^{-1}$; [f] isothermal in 0.2396 M HCl; [g] non-isothermal in 0.2396 M HCl; [h] Connors (1963), his 25°C estimates were converted using $E_1 = 17.13$, $E_2 = 13.98$ $kcal \cdot mol^{-1}$; [i] Eriksen and Stelmach (1965), non-isothermal in 0.982 M HCl, their 25°C estimate was converted using $E_1 = 17.13$ $kcal \cdot mol^{-1}$.

[j] As for i, but their isothermal value.

[k] These values are inflated due to a small contribution from the solvent-catalyzed reaction. After correction values are 1.411 and 1.400 for methods 5 and 6, respectively.

determining factors. For example, for isothermal first-order single pathway kinetics, Eqn. 13 collapses to:

$$\frac{-dA}{dt} = \left(k + \frac{\alpha}{V}\right) \cdot (A - A_b) + k \cdot \epsilon_p \cdot b \cdot \frac{m_\tau}{V} \tag{18}$$

If ionic strength (μ) programming is used, then from the Debye Huckel equation

$$k = k_0 \cdot 10^{(2 \cdot Q \cdot \sqrt{\mu})/(1+\sqrt{\mu})} \tag{19}$$

Then k_0, the rate constant at zero ionic strength, and Q are parameters to be estimated, and μ at any instant (for univalent electrolytes) can be determined as was $[H^+]$. Preliminary experiments using these equations have successfully estimated k_0 and Q.

Conclusions

The kinetic parameters associated with the solvent- and acid-catalyzed hydrolysis of PNPA have been successfully estimated from a single kinetic experiment. This has reduced the experimental workload compared with the traditional isothermal method. This suggests that the effects of other stability determining factors might be estimated in a similar way.

The equipment required for such high information kinetic studies is more complex than for traditional isothermal experiments. Additionally, the data handling requires sophisticated numerical programmes. However, these experiments were performed with an off-line passive system. With the increasing availability of on-line real-time computer systems, experiments using programmed stability determining factors will become more attractive.

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