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Kinetics by Thermometry: An Aldol Condensation Reaction

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The principles of 'thermokinetic' experiments have been described, whereby the initial rates of chemical reaction in solution are determined by following the temperature rise in an adiabatic system; data are obtained within the first few seconds of mixing, and at rates of the order of one measurement s^{-1}. The procedure has been applied to the base-catalysed condensation reaction of acetone to form diacetone alcohol, an exceptionally difficult reaction to follow because of the small extent to which the reaction proceeds. At 26 °C, the equilibrium constant for the base-catalysed ionisation of acetone has been established as having a value of 1.2(9) l mol^{-1} while the rate constant for the ionic dimerisation has the value $2.5(2) \times 10^{-3}$ mol l^{-1} s^{-1}.

The progress and rate of a chemical reaction may be followed most directly by analysis of samples collected during the reaction. For many reasons, however, this procedure may be awkward, and indirect methods which sample some physical property related to the changing concentration are often more convenient;[1] typical procedures use dilatometry, electrical conductivity, spectrophotometry, *etc.*

An underexploited technique is to follow the temperature rise in an adiabatic system resulting from an enthalpy change during the reaction ('thermokinetics').[2,3] We demonstrate here the value of this technique in a direct study of the aldol condensation of acetone to form 4-hydroxy-4-methylpentan-2-one (diacetone alcohol, DAA). The kinetics of this important reaction have been reported, apparently reliably, only once before[4] using highly sophisticated instrumentation, presumably because the small extent of reaction yields only low concentrations of product for which analysis is extremely difficult. Instead, the reverse reaction has been studied,[1,5,6] and the kinetics of the forward reaction only inferred. By contrast, we demonstrate here the extreme simplicity of both the equipment and the analysis required for thermokinetic study of the forward reaction, yielding a rather full description of the kinetics of the reaction and drawing into question the earlier report.[4] The technique is widely applicable to reactions involving solutions and even to heterogeneous systems.

Thermokinetic Reaction

Aldol condensation is an important class of reaction used in organic synthesis for the production of valuable chemical products: unsaturated aldehydes, dienes and aldo- and keto-alcohols. The condensation of acetone to form DAA is given by:

$$2CH_3{-}CO{-}CH_3 \rightarrow (CH_3)_2{-}C(OH){-}CH_2{-}CO{-}CH_3$$

Under ambient conditions (room temperature and pressure), this reaction is very slow (after all, acetone is a common solvent), but is accelerated by base catalysis. In the present case, we use aqueous sodium hydroxide as the catalyst, and determine the initial rate of reaction at various aqueous concentrations of the acetone and at various catalyst concentrations. The reaction has an only moderate enthalpy change ($\Delta_r H = -30.6$ kJ mol^{-1}) (see Appendix), which, however, proves to be sufficient to follow the reaction even in reasonably dilute solution.

Experimental

Equipment and Calibration

The reaction is performed within a covered vacuum (Dewar) flask of about 100 ml capacity, fitted with a glass stirrer. Temperature is followed by means of a thermistor of about 80 kΩ room-temperature resistance; the resistance value is digitized in arbitrary units *via* a computer (8-bit resolution), averaged (50 values in every 3 s), and converted to temperature by reference to the 'thermistor equation':

$$R = A \exp(B/T)$$

where R is the measured resistance and T the absolute temperature. The two constants, A and B, are determined for the thermistor/computer system by calibration against a sensitive thermometer at two temperatures straddling the temperatures encountered over the period of the reaction.

Experimental Procedure

The reaction mixtures consist of aqueous solutions of acetone of varying concentrations. The mixtures were prepared in 300 ml quantities, of which 80 ml were used per run, and were allowed to equilibrate in a constant temperature bath before use in order that the enthalpy of mixing might dissipate.

The temperature-equilibrated reaction sample was placed in the vacuum flask, the thermistor inserted through the cover, the stirrer started, and the computer set to collect and record the temperatures at regular intervals.

The temperature was followed for a short time (about 5 min), to establish an initial temperature/time gradient, then 2 ml of temperature-equilibrated catalyst solution were added by pipette, and the temperature again followed for a similar 5–10 min period.

The recorded temperatures (see Fig. 1) are fitted by a straight line to the initial data (before addition of the catalyst solution), and by a low-order polynomial to the early data for

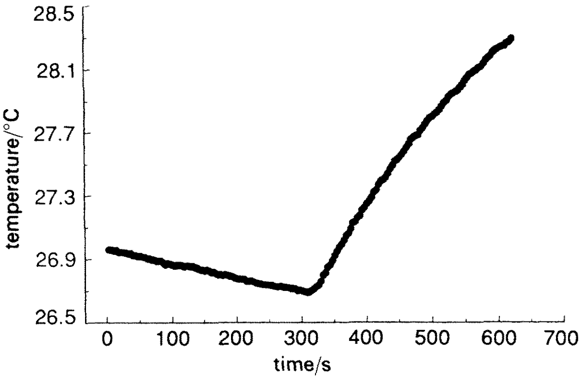

Fig. 1 Temperature–time graph of an acetone (55 ml)–water (25 ml) mixture before and after addition of 2 ml of 4 mol l^{-1} NaOH catalyst

Table 1 Kinetic results for the condensation reaction of acetone[a] at 26 °C

OH^-/mol	$[OH^-]$/mol l^{-1}	V_A/ml	$\Delta(d\theta/dt)^b/10^3$ degree s^{-1} (duplicate runs)	
0.0060	0.07(6)	55	5.61	5.77
		50	4.43	4.53
		45	3.45	3.15
		40	2.36	2.31
		35	1.77	—
		33	1.37	1.38
		30	1.37	1.38
		27	0.81	0.84
0.0080	0.10(1)	55	8.25	8.05
		50	6.04	6.10
		45	4.27	4.37
		40	3.05	3.10
		35	2.19	2.25
		33	2.01	1.99
		30	1.47	1.53
		27	1.11	1.16

[a] Volumes of components in reaction mixture: 2.00 ml of NaOH (3 or 4 mol l^{-1}); V_A ml of acetone; $(80.0 - V_A)$ ml of distilled water. The range of catalyst concentration was limited at the high end by the limited solubility of NaOH in acetone solution and, at the low end by the slowness of the resultant catalysed reaction. [b] Difference of slopes before and after addition of 2 ml of catalyst.

the mixture with catalyst (about 10 data points are fitted by a quadratic). The difference in temperature *vs.* time slopes at the time of addition of the catalyst (which process disturbs the captured data for very few data points) constitutes a measure of the initial rate of the chemical reaction.

Although the digitizer has only 8-bit resolution and a kinetic run with a temperature change of 0.5 to 1 °C uses only a small fraction of the available range, the 50-point average provides an excellent effective resolution, as shown by the recorded curves (Fig. 1). Furthermore, since we fit the averaged data points by means of low-order polynomials (using only the initial portion of the data), we enhance the resolution of our slopes. Initial rates of temperature rise are in the region of $(1.0 \pm 0.05) \times 10^{-3}$ °C s^{-1}, where this reported 'within-run' standard error is obtained from the statistical fitting procedure. Of course, 'between-run' precision will be worse, depending also on concentration inaccuracies and other uncontrolled experimental features. We estimate an experimental precision of 0.1×10^{-3} °C s^{-1} from the internal evidence of our duplicate and triplicate runs (*cf.* Table 1).

A few aspects of this experimental procedure are worthy of consideration, since here a rate constant whose value changes with temperature is determined by following a temperature rise. (*a*) The temperature rise is kept small, and the reaction is performed under nearly adiabatic conditions in a vacuum flask, so minimizing heat losses. (*b*) The initial rate used is the difference between the slopes before and after addition of catalyst, so correcting for common heat transfers. (*c*) The effective temperature rise is very small, since only the initial rate (corrected) is used in the analysis, and this temperature rise is comparable to the fluctuations in temperature encountered during a standard isothermal kinetic experiment. (*d*) The very low heat capacity of the thermistor, and its consequent rapid response, ensures that it does not introduce an artefactual time constant into the rate determinations.

Theory of the Method

The rate of flow of heat between the reactor (vacuum flask) and its environment, in the absence of reaction, can be written as follows:

$$\sum C_i \frac{d\theta_1}{dt} = Q - \lambda(\theta_1 - \theta_{env}) \tag{1}$$

where θ_1 is the temperature in the reactor, θ_{env} is the temperature of the environment, Q is the rate of heat generation by the stirrer, λ is the heat transfer coefficient, and $\sum C_i$ is the total heat capacity of the reactor and contents which is equal to $(C_f + C_m)$ where C_f is the heat capacity of the flask and stirrer and C_m is the heat capacity of the reaction mixture.

In the presence of a reaction, the equation becomes:

$$\sum C_i \frac{d\theta_2}{dt} = Q - \lambda(\theta_2 - \theta_{env}) - \Delta_r H \frac{dn}{dt} \tag{2}$$

where θ_2 is the temperature of the reactor during reaction, $\Delta_r H$ is the enthalpy of reaction (the sign of the term is negative because enthalpy released in the reaction is taken up by the reactor and its contents), n is the instantaneous amount of the reagent to which the enthalpy of reaction is referred and dn/dt is the corresponding rate of conversion of this reagent.

Subtracting eqn. (1) from (2), we obtain the influence of the reaction alone:

$$\sum C_i \Delta\left(\frac{d\theta}{dt}\right) = -\Delta_r H \frac{dn}{dt} - \lambda \Delta\theta \tag{3}$$

where

$$\Delta\theta = \theta_2 - \theta_1$$

and

$$\Delta\left(\frac{d\theta}{dt}\right) = \frac{d\theta_2}{dt} - \frac{d\theta_1}{dt}$$

The reaction rate is studied at the start of the reaction ('initial rate' method) where the rate terms are $\Delta(d\theta/dt)_0$ and $(dn/dt)_0$, and $\Delta\theta = 0$. Therefore,

$$\left(\frac{dn}{dt}\right)_0 = -\left(\frac{\sum C_i}{\Delta_r H}\right)\Delta\left(\frac{d\theta}{dt}\right)_0 \tag{4}$$

The chemical rate law is, however, generally expressed in concentration terms:

$$r \equiv -\frac{dc}{dt} \tag{5}$$

Hence, eqn. (4) needs to be converted into an expression in terms of concentration, corresponding to eqn. (5).

If the volume, V, is constant during this liquid-state reaction (and this is certainly true for low conversion of the reagent), then:

$$\frac{dn}{dt} = -V \frac{dc}{dt} \tag{6}$$

Therefore, substituting eqn. (6) into eqn. (4):

$$\left(\frac{dc}{dt}\right)_0 = \left(\frac{\sum C_i}{V \Delta_r H}\right)\Delta\left(\frac{d\theta}{dt}\right)_0 \tag{7}$$

Eqn. (7) provides a link between the experimental data and the required results, in the form of eqn. (5), provided that the various constants are known.

Reaction Mechanism and Kinetic Constants

The base-catalysed aldol condensation of acetone (A) to diacetone alcohol (DAA) has been rather thoroughly examined,

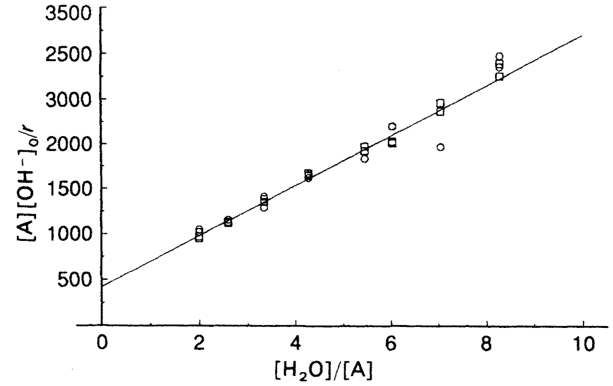

Fig. 2 [A][OH$^-$]$_0$/rate *vs.* [H$_2$O]/[A] for acetone–water mixtures at 26 °C, with additions of 2 ml of 3 mol l^{-1} (○) and 4 mol l^{-1} (□) NaOH. A linear least-squares fit to the 31 data points yields an intercept of 419 (with a standard deviation of the estimate of 61) and a slope of 278 (±12), in the units of the plot. Addition of a further 80 data points from a first set of runs, with additions of 2 ml of 2, 3 and 4 mol l^{-1} NaOH, yields a linear least-squares intercept of 396 (±56) and a slope of 306 (±11); we use the latter, slightly more reliable, values for determining the kinetic constants of the reaction.

and is believed to occur *via* the following mechanism:[1]

$$\mathrm{A + OH^-} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{A^- + H_2O} \qquad \textbf{(A)}$$

$$\mathrm{A^- + A} \xrightarrow{k_2} \mathrm{DAA^-} \qquad \textbf{(B)}$$

$$\mathrm{DAA^- + H_2O} \xrightarrow{k_3} \mathrm{DAA + OH^-} \qquad \textbf{(C)}$$

where equilibrium in step **(A)** is rapidly achieved, step **(B)** is assumed to be the rate-limiting step, and step **(C)** occurs rapidly.

Using the steady-state approximation (d[A$^-$]/dt = 0), with the accompanying assumption that DAA$^-$ is produced in the rate-limiting step, but rapidly removed (*i.e.*, [DAA$^-$] ≪ [A$^-$] + [OH$^-$]), we find that:

$$[\mathrm{A^-}] = \frac{k_1[\mathrm{A}][\mathrm{OH^-}]_0}{k_{-1}[\mathrm{H_2O}] + (k_1 + k_2)[\mathrm{A}]}$$

where [OH$^-$]$_0$ = [OH$^-$] + [A$^-$].

The rate (r) of formation of product, DAA, is controlled by the rate-limiting step **(B)** in the steady-state approximation:

$$r = k_2[\mathrm{A^-}][\mathrm{A}] = \frac{k_1 k_2[\mathrm{A}]^2[\mathrm{OH^-}]_0}{k_{-1}[\mathrm{H_2O}] + (k_1 + k_2)[\mathrm{A}]} \qquad (9)$$

which may be written in a linearised form as:

$$\frac{[\mathrm{A}][\mathrm{OH^-}]_0}{r} = \frac{k_{-1}}{k_1 k_2}\frac{[\mathrm{H_2O}]}{[\mathrm{A}]} + \frac{(k_1 + k_2)}{k_1 k_2} \qquad (9')$$

The chemical rate of reaction may be substituted by experimental quantities from eqn. (7):

$$r = \left(\frac{\sum C_i}{V\Delta_r H}\right) r_\theta \qquad (7')$$

where

$$r_\theta = \Delta\left(\frac{\mathrm{d}\theta}{\mathrm{d}t}\right)_0$$

Hence, a plot of [A][OH$^-$]$_0$/r *vs.* [H$_2$O]/[A] should yield a straight line with slope $m = k_{-1}/(k_1 k_2)$ and intercept $c = (k_1 + k_2)/(k_1 k_2)$ (see Fig. 2). If we assume step **(B)** to be rate-limiting, so that $k_1 \gg k_2$, then:

$$k_2 = 1/c$$

and also:

$$c/m = (k_1 + k_2)/k_{-1} \approx k_1/k_{-1} = K_c^{\mathrm{A}}$$

where K_c^{A} is the equilibrium constant of reaction (**A**).

The kinetic quantities required for the evaluation of k_2 and of K_c^{A} are determined directly from our experiments [with concentrations corrected for the density change on mixing (at 25 °C)];[7] the heat capacity of the flask and stirrer (48 J K^{-1}) is determined by the standard method of following the temperature change on adding hot water; to this value is added the heat capacity of the mixture (at 17 °C);[8] the enthalpy of reaction, $\Delta_r H$, is from the literature (see Appendix) (each uncorrected for concentration and temperature effects, which are expected to be small in this case).

Results and Discussion

Table 1 and Fig. 2 display our derived results. Fig. 2 demonstrates good linearity indicating that the mechanism proposed is consistent with the experiment. Table 1 contains our kinetic results. At 26 °C, the equilibrium constant for the ionisation of acetone is 1.2(9) l mol^{-1}, and the rate constant for the assumed rate-limiting step **(B)** is 2.5(2) × 10^{-3} mol l^{-1} s^{-1} (see caption to Fig. 2 for details).

We may compare our results and those of earlier workers[1,5,6] from their reported equilibrium constants and rate constants for the back reaction. These yield overall second-order ('apparent') rate constants divided by hydroxy concentration for the forward reaction of 17.3 × 10^{-3} l^2 mol^{-2} min^{-1} for dilute acetone solution (80% water) and 11.3 × 10^{-3} l^2 mol^{-2} min^{-1} for concentrated acetone solution (4% water). Our own (pure acetone) directly obtained limiting value is 10.5 × 10^{-3} l^2 mol^{-2} min^{-1}, which matches the classical results rather well.

However, comparison with the only other apparently reliable direct measurement is rather more problematic. First, Maple and Allerhand[4] used the results of an exponential curve-fit to experimental data, which is notoriously subject to error because of uncertainty in the long-time results (their Fig. 3 shows only 24 of their reported 27 results). Secondly, their exponential equation arose from an incomplete mechanism, omitting the effect of catalyst, the consequences of which are difficult to evaluate in terms of the 'apparent' rate-constants which result. However, if we accept their data for acetone in water–cyclohexane solutions, and approximate their results to our mechanism, we find an apparent forward rate constant of 2.5 × 10^{-3} l^2 mol^{-2} min^{-1}, which is a factor of four slower than the other results reported. We are unable to provide an explanation for this discrepancy. We discount entirely a report[9] which purports to show that DAA is obtained from the reaction in 90% yield at room temperature.

Summary

We describe a thermokinetic procedure for following the initial rates of solution reactions, and have applied the procedure to the otherwise exceptionally difficult condensation reaction of acetone. We show that this reaction (which proceeds to only *ca.* 1% completion) can be dealt with quite readily by thermokinetics. We have confirmed the proposed mechanism at 26 °C, and have determined certain of the kinetic constants. Our results are in agreement with earlier results derived from the back reaction, but now provide detailed mechanistic values for the forward reaction.

The present procedure provides data at rates better than two orders of magnitude faster than earlier methods: classical procedures, suitable for the back reaction only,[1] require 5–10 min per data point; the elaborate NMR procedure for the forward reaction[4] requires $3\frac{1}{2}$ min per data point; our thermokinetic procedure yields results at a rate of the order of seconds per data point. Furthermore, we obtain data at a very early stage of the reaction, within a few seconds of mixing, before side- and back-reactions can have any appreciable influence.

Appendix

Reaction Enthalpy, $\Delta_r H$

The standard enthalpy of the reaction:

$$2\text{A(aq)} \longrightarrow \text{DAA(aq)}$$

(where 'aq' represents aqueous solution) may be calculated in a number of ways.

The direct calculation, by difference of the standard enthalpies of the liquid components,[10,11] yields a value of -96.6 kJ mol^{-1}. This applies to the pure components and, as the difference of two much larger quantities, is subject to possible error.

We prefer to evaluate $\Delta_r H$ more directly from the equilibrium constant, K, for the reaction. Three values of K are available to us: 0.006 l mol^{-1} at 26.5 °C,[4] 0.032 l mol^{-1} at 25 °C,[5] and 0.0714 l mol^{-1} at 25 °C.[12] We reject the first because of inconsistencies with other kinetic results (see our Results and Discussion section), while the third value was obtained in the absence of water; we judge the second value to be the more relevant. It follows from this value, and the entropy of reaction for the pure liquids:[10,13] $\Delta_r S^\ominus = -131.1$ J K^{-1} mol^{-1} that

$$\Delta_r H = -30.6 \text{ kJ mol}^{-1}$$

In contrast, the first equilibrium constant yields $\Delta_r H = -26.4$ kJ mol^{-1}, and the third $\Delta_r H = -32.5$ kJ mol^{-1}. Note that these are not widely different, but all differ considerably from the simple difference of enthalpies of formation which is indicated above.

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