An Isochoric Probe of the Role of Solvent Structure in the Kinetics of Neutral Hydrolysis of Two 1-Acyl-1,2,4-Triazoles in Aqueous Solution

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Kinetic data for the neutral hydrolysis in aqueous solutions of 1-acetyl-1,2,4-triazole and 1-benzoyl-3-phenyl-1,2,4-triazole have been analysed to yield the dependences of rate constants on temperature under isobaric and isochoric conditions. The latter condition requires that the pressure changes to hold the molar volume of water constant and equal to that at 298.15 K and 101 325 N m^{-2}. The contrasts in the dependence of rate constants probes the role of solvent in the activation process. In these two cases, the rate constants increase with increase in temperature more rapidly under isochoric than isobaric conditions, a trend consistent with a decrease in hydrophobic character on activation, and production of labile water molecules resulting from disruption of water–water interactions.

In 1935 Evans and Polanyi noted[1] how the problem of understanding the role of solute–solvent interactions in chemical reactions would be simplified if the temperature dependence of rate constants could be measured at constant volume. This ostensibly simple proposal has aroused considerable debate,[2,3] stimulated by attempts to put it into practice. Nevertheless, it is now clear that the isochoric condition refers to the solvent rather than the solution and that the way forward develops the argument along the lines discussed[4,5] by Marshall with regard to equilibrium constants for chemical equilibria in solutions. Within the present context, data describing the dependences of rate constants on temperature and pressure are analysed to obtain kinetic parameters at selected temperatures and pressures for which the molar volume of the solvent is constant. Previously[3] we showed how for reactions in aqueous solutions, kinetic data can be analysed to obtain parameters characterising reactions under conditions in which the molar volume of water[6] equals that at 298.15 K and ambient pressure, 101 325 N m^{-2}. In this paper we report an analysis of kinetic data describing the neutral hydrolysis of two triazoles.[2] These are interesting reactions because the transition states are less hydrophobic than the initial states. The mechanism (for the Scheme see ref. 2) of the hydrolysis of these activated amides in the pH range 3–6 involves water-catalysed nucleophilic attack by water at the carbonyl group. The reaction is bimolecular in water and therefore trimolecular overall. A useful comparison is drawn with kinetic data describing the aquation of an iron(II) complex cation, where activation produces a more hydrophobic solute. We draw attention to the difference between calculated isobaric and isochoric dependences of rate constants on temperature. The difference is used as a basis for comments on the role of solvent and hence the mechanism of reaction.

Table. Parameters describing the dependences on temperature and pressure of rate constants for the neutral hydrolysis of two 1-acyl-1,2,4-triazoles in aqueous solution.

Parameter	Substrate (**1**)	Substrate (**2**)
θ/K	298.15	298.15
$\pi/10^8$ N m^{-2}	1.0015	1.0015
a_1	-11.118 ± 0.011	-11.675 ± 0.018
a_2	15.50 ± 0.60	17.18 ± 0.90
a_3	0.6821 ± 0.014	0.689 ± 0.021
st. error	3.826×10^{-2}	4.96×10^{-2}
$\Delta^{\ddagger}H^{\infty}(\theta; \pi)$/kJ mol^{-1}	38.68	42.59
$\Delta^{\ddagger}V^{\infty}(\theta; \pi)$/cm^3 mol^{-1}	-16.9	-17.06

Analysis.—For the hydrolysis of 1-acetyl-1,2,4-triazole (**1**), the kinetic data describe the dependences of rate constants on temperature and pressure over the range $292.348 \leqslant T/\text{K} \leqslant 309.74$, and $1.013\,25 \leqslant p/10^5 \text{ N m}^{-2} \leqslant 2.001 \times 10^3$ respectively. For the hydrolysis of 1-benzoyl-3-phenyl-1,2,4-triazole (**2**), the corresponding ranges are $292.18 \leqslant T/\text{K} \leqslant 309.70$, and $1.013\,25 \leqslant p/10^5 \text{ N m}^{-2} \leqslant 2.0010 \times 10^3$. Substrate (**2**) is more hydrophobic than substrate (**1**). The kinetic data were obtained[2] by measuring the decrease in absorbance with time at 222 nm for substrate (**1**) and 273 nm for substrate (**2**) in aqueous solutions containing 10^{-3} mol dm^{-3} HCl, to prevent alkaline hydrolysis of the esters. These kinetic data were fitted to equation (1) where θ and π are reference temperature and pressure, respectively.[7]

$$\ln (k/T) = a_1 + a_2[(T - \theta)/\theta] + a_3[(p - \pi)/\pi] \quad (1)$$

Here a_1 equals $\ln (k/T)$ at (θ, π). We fitted the dependence of $\ln (k/T)$ rather than $\ln k$ thereby taking account[7] of transition-state theory. The impact on the plots discussed below is marginal as $\ln T$ is close to a linear function of T over small temperature ranges.[7] In a separate analysis we used the equation and parameters reported by Fine and Millero[6] to calculate temperature–pressure pairs $(T, p)^v$ at which the molar volume of water equals that at 298.2 K and 101 325 N m^{-2}.

Results

The kinetic data, in conjunction with equation (1), yield the parameters reported in the Table. These estimates were used to obtain two sets of rate constants for each substrate. The first set comprised the isobaric dependence of rate constants on temperature over the measured temperature range and at ambient pressure. The second set comprised rate constants as a function of temperature but at pressures calculated to conform to the isochoric conditions discussed above (Figure). For both substrates, the rate constants increase more rapidly under isochoric conditions.

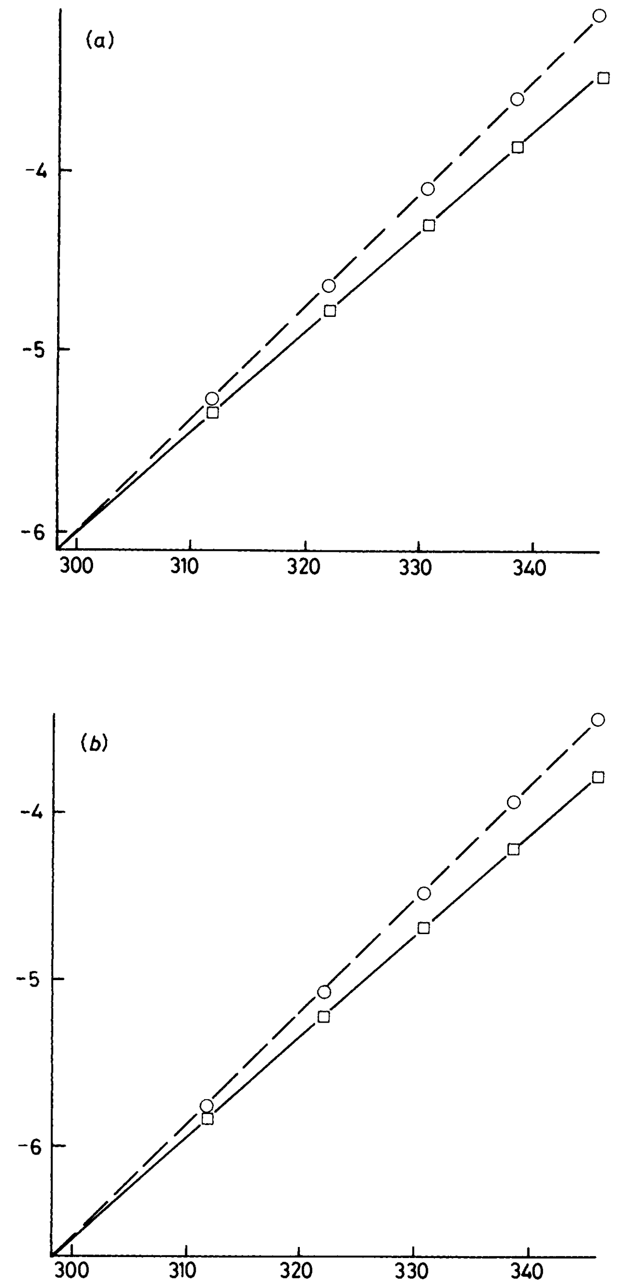

Figure. Dependences of rate constants on temperature for neutral hydrolysis. (*a*) 1-acetyl-1,2,4-triazole (**1**); (*b*) 1-benzoyl-3-phenyl-1,2,4-triazole under: (□), isobaric conditions; (○), isochoric conditions. (The points refer to calculated $\ln(k/T)$ under isobaric and isochoric conditions.)

Discussion

According to the mechanism[2] for hydrolysis of substrates (**1**) and (**2**), the solvent water provides the medium for reaction and is directly involved in the chemical reaction. In order to understand both roles we recall the Lumry model[8] for liquid water which uses a two-state description. Thus at fixed T and p, water molecules are involved in either strong hydrogen-bonded, high-volume clusters or weak hydrogen-bonded, dense clusters. Increases in temperature and/or pressure favour the weak hydrogen-bonded state. In terms of the Symons model[9,10] for water, there is an increase in the concentration of chemically reactive free OH groups. The patterns formed by the calculated rate constants in the Figure can be understood in these terms.

Hydrophobic solutes enhance neighbouring water–water interactions, which increases the proportion of water molecules involved in strong hydrogen bonds. If reaction and activation require disruption or weakening of water–water interactions, hydrophobic hydration inhibits the chemical reaction. With increase in temperature (above the temperature of maximum density), the isochoric condition requires that the pressure increases to hold the molar volume constant. Hence the extent of disruption of water–water interactions which occurs with an increase in temperature is larger under isochoric than under isobaric conditions. Nevertheless, in the isochoric case the mean water–water distance remains constant. The enhanced isochoric disruption of water–water interactions produces an increase in the rate constant at a given temperature on going from isobaric to isochoric conditions. The trend is enhanced by the increased lability of the water molecules in the hydrolysis reaction.

A reverse trend is observed[3] in the aquation of the iron(II) complex* cations $[\mathrm{Fe(phen)_3}]^{2+}$. In other words, the rate constant falls on going from isobaric to isochoric conditions at fixed temperature, consistent with a mechanism in which the substrate cations become more hydrophobic on activation, a consequence of the stretching of Fe–N bonds and increased exposure of the hydrophobic ligands to the solvent. The change in hydrophobic character is more important for this substrate in that isochoric breakdown of water–water interactions is unfavourable to the hydration changes in the activation process.

These calculations point to an interesting method for testing the mechanisms of reaction in terms of the extent to which it takes account of the role of the solvent.

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* phen = 1,10-phenanthroline.