Kinetics of hydrolysis in aqueous solution of 1-benzoyl-1,2,4-triazole; the role of pairwise and triplet Gibbs energy interaction parameters in describing the effects of added salts and added alcohols

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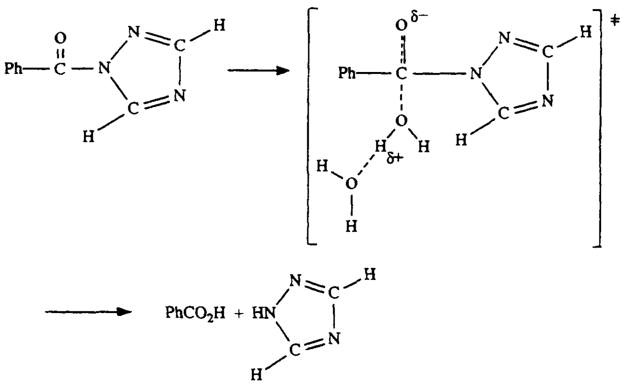
Kinetic data are reported for the spontaneous hydrolysis of 1-benzoyl-1,2,4-triazole in aqueous solutions at ambient pressure and 298.2 K, in aqueous solutions containing added ethanol, propanol and sodium chloride. Kinetic data are also reported for the same reaction in aqueous mixtures of sodium chloride and ethanol. When either ethanol or propanol are added the rate constant k decreases, plots of $\ln(k)$ *vs.* molality of alcohol being linear. The patterns are accounted for using pairwise Gibbs energy interaction parameters. The rate constant k decreases more dramatically when sodium chloride is added. This pattern is accounted for using pairwise and triplet interaction parameters. The dependence of rate constant on molality of added ethanol in solutions containing fixed molalities of sodium chloride deviates from that predicted using the pairwise interaction parameters indicating a non-additivity of salt and alcohol effects on the rate constant. The deviations increase with increase in molalities of both added salt and added solvent in a direction consistent with a disruption of the substrate–alcohol hydrophobic interactions by added salt.

Rate constants describing the spontaneous hydrolysis of organic substrates in aqueous solutions are particularly sensitive to the amounts and nature of added organic co-solutes/co-solvents. Classically, these changes in rate constants can be understood in terms of changes in polarity of the substrate on going from initial to transition states[1] linked to the change in polarity of the solvent. The latter can be measured in many ways,[2] the definition of E_T values by Reichardt[3] being particularly useful. For aqueous solutions, the hydrophobic/hydrophilic character of substrate and added solute are important considerations, particularly the role of hydrophobic hydration.[4,5] The rate constants for the class of spontaneous hydrolysis reactions considered here generally decrease when organic solutes are added.[6,7] This pattern emerges where the transition states are less hydrophobic than the initial states. The effect of, for example, added ethanol on the rate constant for the hydrolysis of an organic ester can be understood in terms of overlap of Gurney cospheres[8] involving the solute ethanol and, in turn, the initial and transition states.[1] Analysis of the data indicates that the hydrophobic co-solute ethanol stabilises the hydrophobic initial state of the substrate ester. A quantitative analysis of these co-solute effects was formulated in terms of pairwise solute–solute interaction parameters. This form of analysis has its origins in the analysis of solvent activity coefficients given by Knight, Kozak and Kauzmann.[9] In an extension of the Savage–Wood treatment,[10] the effect of an added co-solute on the rate constant is re-expressed in terms of pairwise Gibbs energy interaction parameters.[11,12]

This approach accounts satisfactorily for trends in rate constants for solvolytic reactions where the added co-solutes include urea, substituted ureas,[11,12] alcohols,[13–15] carbohydrates,[14] carboxamides,[16,17] sulfones,[17] sulfonamides[17] and sulfoxides.[17] The validity of the approach, based on pairwise group interaction parameters, is confirmed therefore for a gallimaufry of co-solute effects in which key roles are assigned to pairwise group interactions although in the case of added carbohydrates[14] account must be taken of stereochemical features.

Here we show that the effect on the rate constant for the hydrolysis of 1-benzoyl-1,2,4-triazole in aqueous solution of added ethanol or propanol fits the pattern described above. These effects are compared with the effect of adding sodium chloride. In the latter case, the dependence of $\ln(k)$ on molality of added salt is non-linear. A satisfactory description of these kinetic salt effects requires terms which are linear and quadratic in molality of added salt leading to pairwise and triplet interaction parameters. These data form the basis of an investigation into the kinetics of hydrolysis of 1-benzoyl-1,2,4-triazole in aqueous solutions containing both added sodium chloride and ethanol. We compare the observed dependence on the rate constant for hydrolysis (Scheme 1) in aqueous salt solutions on molality of added alcohol. We show that the effects of the alcohol are not accounted for using the previously derived pairwise interaction parameters.



Scheme 1

Experimental

Materials

1-Benzoyl-1,2,4-triazole was prepared using the procedures described previously.[18–20] All solutions were prepared by mass and contained HCl (aq; 10^{-4} mol dm^{-3}) to suppress catalysis by hydroxide ions. The pH of the solutions was held within the range 3.9 to 4.1. The alcohols and sodium chloride (fresh p.a. grade from Merck Chemicals) were used as supplied.

Kinetic measurements

Rates of chemical reaction were followed[15] by measuring the dependence on time of the absorbance at 250 nm using a Perkin-Elmer Lambda 2 UV–VIS spectrophotometer. Reactions were followed for at least four half-lives at 298.15 ± 0.15 K. Rate constants were reproducible to within ±1% and were calculated using a data station attached to the spectrophotometer. Complimentary experiments using as substrate 1-benzoyl-3-phenyl-1,2,4-triazole showed that alcoholysis contributed less than 4% of the overall reaction when ethanol was added.[21]

Results

In aqueous solution the first-order rate constant for hydrolysis of 1-benzoyl-1,2,4-triazole (Scheme 1) is 2.06×10^{-3} s^{-1} at 298.2 K and ambient pressure. When either ethanol or propanol was added the rate constant decreased (Table 1). When sodium chloride was added the rate constant also decreased but, on the basis of salt molality, the change in rate constant was more dramatic; Table 2. The main objective of the study reported here is an analysis of the set of data given in Table 2 which records the dependence of the first-order rate constant for the hydrolysis reaction (Scheme 1) on the molality of ethanol, m_a, and molality of sodium chloride, m_s, in aqueous solutions containing both salt and alcohol. Again the rate constant for hydrolysis decreases when both m_a and m_s increase. We return to the patterns below.

Table 1 Dependence of rate constant for hydrolysis of 1-benzoyl-1,2,4-triazole on molality of added alcohol, m_a

	m_a/mol kg^{-1}	$k/10^{-3}$ s^{-1}
Ethanol	0.266	2.00
	0.515	1.94
	0.811	1.88
	1.060	1.83
	1.206	1.80
	1.39	1.76
Propanol	0.340	1.93
	0.496	1.89
	0.653	1.84
	1.049	1.71
	1.232	1.66
	1.479	1.58

Table 2 Dependence of first order rate constant on molality of added sodium chloride for the hydrolysis of 1-benzoyl-1,2,4-triazole in aqueous solution

m_s/mol kg^{-1}	$k/10^{-3}$ s^{-1}
0.514	1.82
1.063	1.57
1.642	1.30
2.264	1.06
2.931	0.838
3.637	0.685
4.404	0.468

Analysis of kinetic data

Neutral solutes. For an aqueous solution containing solute-i and solute-j in 1 kg of water at fixed temperature and fixed pressure, the excess Gibbs energy G^E is defined using eqn. (1).

$$G^E/RT = (1 - \varphi)(m_i + m_j) + m_i \ln \gamma_i + m_j \ln \gamma_j \quad (1)$$

Here φ is the practical osmotic coefficient; γ_i and γ_j are the activity coefficients of the solutes. Deviations from ideal in the properties of the dilute solution can also be described using pairwise Gibbs energy interaction parameters; eqn. (2), where

$$G^E = g_{ii}(m_i/m^\circ)^2 + 2g_{ij}m_i m_j/(m^\circ)^2 + g_{jj}(m_j/m^\circ)^2 \quad (2)$$

m° is the standard molality, 1 mol kg^{-1}. In the limit that solute-j is present in only trace amounts, the corresponding trace activity coefficient γ_j^T is related[7,12] to molality m_i using eqn. (3). This quintessentially extrathermodynamic analysis centres

$$\ln \gamma_j^T = 2g_{ij}m_i/RT(m^\circ)^2 \quad (3)$$

attention on g_{ij}, a pairwise interaction parameter which describes how solute-i perturbs the properties of solute-j. If solute-j models in turn the initial and transition states of the substrate in a reaction described as first-order in substrate then the ratio γ_{is}/γ_{ts} is given by eqn. (4), where the Gibbs energy

$$\ln(\gamma_{is}/\gamma_{ts}) = 2G^P(C)m_i/RT(m^\circ)^2 \quad (4)$$

interaction term describing the effect of a co-solute is given in eqn. (5). In eqn. (5), $g(is \leftrightarrow i)$ and $g(ts \leftrightarrow i)$ are pairwise

$$G^P(C) = g(is \leftrightarrow i) - g(ts \leftrightarrow i) \quad (5)$$

interaction parameters for the inital and transition states respectively. Then in the limit that the corresponding molalities m(is) and m(ts) tend to zero, eqn. (6) applies. Here n is the

$$\ln[k/k(\text{id})] = 2G^P(C)m_i/RT(m^\circ)^2 - \varphi n M_1 m_i \quad (6)$$

number of water molecules involved on forming the transition state and equals 2 for the system discussed here (see Scheme 1). For dilute aqueous solutions φ is approximately unity. The analysis outlined above is readily extended to include a triplet interaction term, $G^T(S)$. In the treatment of the kinetic data, we defined a quantity Q using eqn. (7). Then the data were fitted

$$Q = \ln[k(m_a)/k(m_a = 0)] + 2M_1 m_a \quad (7)$$

to eqn. (8) using a linear least squares analysis.

$$Q = a_1 + [2G^P(C)/RT(m^\circ)^2]m_a + [3G^T(C)/RT(m^\circ)^3](m_a)^2 \quad (8)$$

For solutions containing ethanol, $G^P(C)$ equals −98.5 ± 4.3 J kg^{-1} but the triplet term and the a_1 term are small and statistically insignificant. [The small a_1 parameter simply means that the curve described by eqn. (8) passes through the origin.] For solutions containing propanol a similar pattern emerged with $G^P(C)$ equal to −158 ± 14 J kg^{-1}. The dependences of calculated and observed Q values [eqn. (8)] are compared for both ethanol and propanol solutions in Fig. 1. Thus, for both monohydric alcohols $G(C)$ is negative. Following the patterns described previously,[7,11–17] we account for this pattern in terms of stabilisation of the hydrophobic initial state by the added hydrophobic alcohol.

Salt solutions. Here we consider the properties of a solution containing model neutral solute-j, molality m_j, and a salt where the molalities of ions (assuming complete dissociation of the salt) are m_+ and m_-. Then, for example, the chemical potential of the water in the aqueous solution μ_1(aq) is given by eqn. (9).

$$\mu_1(\text{aq}) = \mu_1^*(l) - \varphi RTM_1(m_+ + m_- + m_j) \quad (9)$$

Here $\mu_1^*(l)$ is the chemical potential of liquid water at the

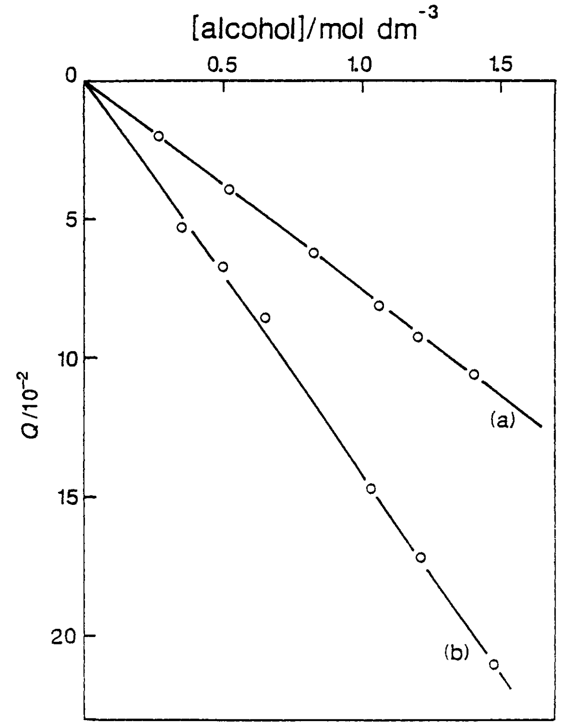


Fig. 1 Comparison of the dependence of Q(calc) (full line) and Q(obs) [*cf.* eqns. (7) and (8)] for the spontaneous hydrolysis of 1-benzoyl-1,2,4-triazole in aqueous solutions containing (*a*) ethanol and (*b*) propanol

same temperature and pressure; M_1 is the molar mass of water. The excess Gibbs energy of a solution in 1 kg of water is expressed in terms of both pairwise and triplet interaction terms.[22] Following through the analysis outlined above we obtain the differential dependence of the excess Gibbs energy G^E on molality of solute-j, m_j at constant moialities of cation m_+ and anion m_-; eqn. (10).

$$(dG^E/dm_j)_{m_+,m_-} = 2[g_{+j}m_+ + g_{-j}m_-]/(m^\circ)^2 + [3g_{j++}m_+^2 + 6g_{j+-}m_+m_- + 3g_{j--}m_-^2]/(m^\circ)^3 \quad (10)$$

There is also an 'ionic strength' term which can be included. We explore this point below. At this stage we note that the first bracketed term on the right hand side of eqn. (10) describes pairwise interactions between solute-j and either cations or anions. The second bracketed term on the right hand side describes the role of triplet interactions on the partial differential $(dG^E/dm_j)_{m_+,m_-}$. For a 1 : 1 salt, chemical substance s, $m_s^2 = m_+m_- = m_+^2 = m_-^2$. Therefore, we group the interaction parameters to define pairwise and triplet salt↔j interaction parameters, g^P and g^T, respectively. Then

$$g^P = g_{+j} + g_{-j} \quad (11)$$

$$g^T = g_{j++} + 2g_{j+-} + g_{j--} \quad (12)$$

Hence, [*cf.* eqn. (3)], for solute-j in trace amounts, the corresponding trace activity coefficient,

$$\ln \gamma_j^T = [2g^P/RT(m^\circ)^2]m_s + [3g^T/RT(m^\circ)^3]m_s^2 \quad (13)$$

Again there is an additional term describing ionic strength effects but this term will cancel when we use eqn. (13) to model initial and transition states. Hence in the context of rate constants [*cf.* eqn. (6)]

$$\ln [k(m_s)/k(m_s = 0)] = [2G^P(S)/RT(m^\circ)^2]m_s + [3G^T(S)/RT(m^\circ)^3]m_s^2 - 2n\varphi M_1 m_s \quad (14)$$

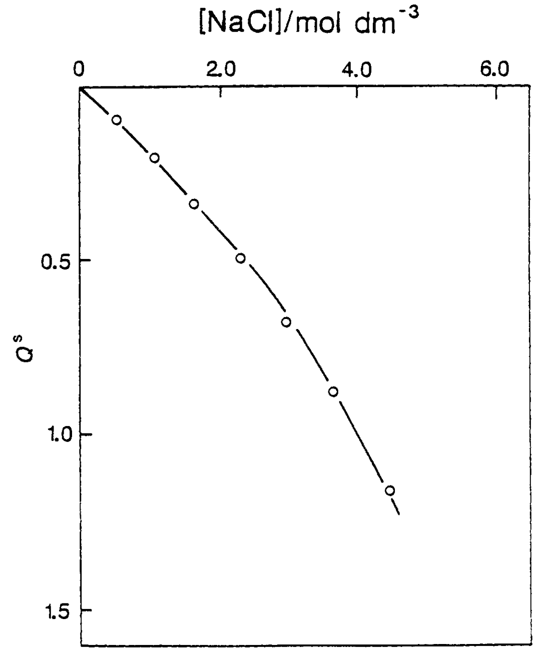


Fig. 2 Comparison of the dependence of Q^S(calc) (full line) and Q^S(obs) defined in eqns. (15) and (16) for the effect of added NaCl on the rate constant for the spontaneous hydrolysis of 1-benzoyl-1,2,4-triazole in aqueous solution at 298.2 K

In eqn. (14), G^P(S) and G^T(S) are the pairwise and triplet kinetic interaction parameters. To analyse the kinetic salt effects we define a quantity Q^S using eqn. (15) [*cf.* eqn. (7)] where m_s is the molality of an added 1 : 1 salt.

$$Q^S = \ln [k(m_s)/k(m_s = 0)] + 4M_1m_s \quad (15)$$

Then [*cf.* eqn. (8)]

$$Q^S = a_1 + [2G^P(S)/RT(m^\circ)^2]m_s + [3G^T(S)/RT(m^\circ)^3]m_s^2 \quad (16)$$

According to the equation the dependence of Q on molality of added salt includes terms linear and quadratic in m_s. For NaCl, G^P(S) equals −212.8 ± 28.8 J kg^{-1} and G^T(S) equals −24.8 ± 6.4 J kg^{-1}. The dependences of Q(calc) and Q(obs) on molality of added sodium chloride are compared in Fig. 2.

Salt solutions + alcohols. The starting hypothesis in this section is that the dependence of rate constant for the studied reaction on solution composition is given by the independent effects of the pairwise interactions involving added alcohol and of both pairwise and triplet interactions involving added salt. In exploring this hypothesis, we used the data summarised in Table 2 to define a quantity Q^{SA} using eqn. (17). Thus, Q^{SA}

$$Q^{SA} = \ln [k(m_s; m_a)/k(m_s; m_a = 0)] + 2M_1m_a \quad (17)$$

describes the effect of adding ethanol, molality m_a, on the rate constant for hydrolysis in an aqueous salt solution, molality m_s, corrected for the effects of alcohol on the chemical potential (reactivity) of water. Therefore, if the effects of added alcohol in terms of solute–solute interactions are independent of the molality of salt, the quantity Q^{SA}(diff) defined in eqn. (18) should be zero irrespective of the molality of added alcohol. Thus

$$Q^{SA}(\text{diff}) = Q^{SA} - [2G(C)/RT(m^\circ)^2]m_a \quad (18)$$

As shown in Fig. 3, the observed dependence of rate constant did not follow the predicted pattern. Thus, Q^{SA}(diff) instead

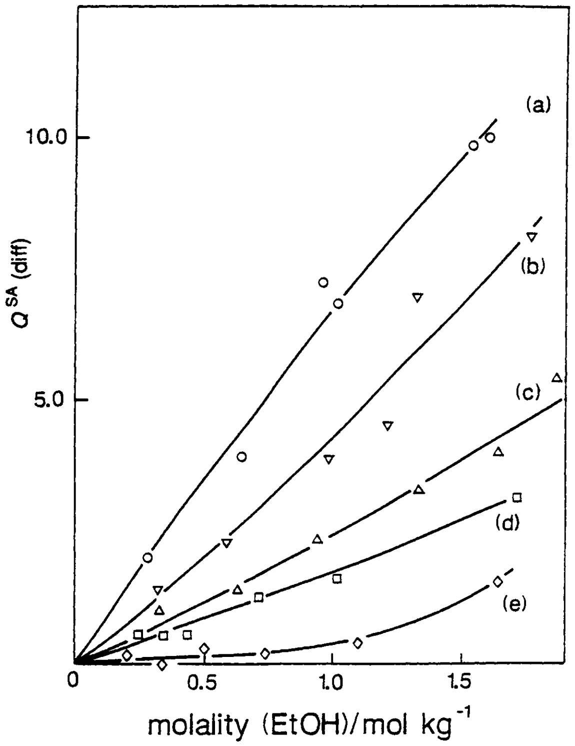


Fig. 3 Dependence on molality of added ethanol of Q^{SA}(diff) defined by eqn. (18) for the spontaneous hydrolysis of 1-benzoyl-1,2,4-triazole in aqueous solutions containing sodium chloride; (*a*) 4.0, (*b*) 3.0, (*c*) 2.0, (*d*) 1.0 and (*e*) 0.15 mol kg^{-1} at 298.2 K. The smooth lines are calculated from the parameters obtained using eqn. (19).

of being zero increased with increase in molality of added ethanol, the increments increasing with increase in molality of added sodium chloride. The pattern was in the direction of a faster rate of reaction than predicted based on simply pairwise additivity. A least-squares analysis of the dependence of Q^{SA}(diff) on molality of added ethanol was explored using eqn. (19). The best fitted curves are shown by the full lines in

$$Q^{SA}(\text{diff}) = a_1 + a_2 m_a + a_3 m_a^2 \qquad (19)$$

Fig. 3. In the five cases shown in Fig. 3, the dominant term expressed Q^{SA}(diff) as a linear function of molality of added alcohol; *e.g.* where m(NaCl) = 4.0, $a_2 = (7.62 \pm 1.2) \times 10^{-2}$ whereas $a_3 = -(7.50 \pm 7.26) \times 10^{-3}$.

Discussion

The study reported above had two aims. First, we wanted to extend the treatments previously outlined[7,11–17] to a consideration of salt effects. We had noted previously that the patterns shown by the dependences of rate constants on molality of added solute could not be satisfactorily accounted for in terms of a decrease in the concentration of water. Thus, added urea increases whereas added dimethylurea decreases the rate constant for spontaneous hydrolysis of *p*-methoxyphenyl dichloroethanoate.[12] Second, we wanted to develop procedures for analysing kinetic data for reactions in aqueous solutions containing both neutral solutes (*e.g.* monohydric alcohols) and salts (*e.g.* sodium chloride). The treatment of kinetic salt effects was against a backdrop of the complexity[23] of the effect of added salts on the solubilities of apolar solutes in aqueous solutions. Nevertheless, we were surprised by the dramatic decrease in rate constant when sodium chloride was added. The dependence of ln $[k(m_S)/k(m_S = 0)]$ on molality of added salt is accounted for in terms of a pairwise interaction parameter with only a modest contribution from a triplet term. It is not possible to assign this kinetic salt effect unambiguously to either changes in chemical potentials, initial or transition state of the substrate. However, the strong hydration of sodium and chloride ions will compete with the requirement for two molecules of water to be involved in the formation of the transition state. This competition will retard the rate of hydrolysis. Our major interest was to assess the extent to which rate constants for reaction in aqueous solutions could be accounted for in terms of the independent effects of added alcohol and salt. There are several ways in which this pattern can be probed. We found the analytical methods based on eqn. (18) to be informative leading to the patterns shown in Fig. 3. The kinetic data show that the effects of added salt and added alcohol are not additive. This result is not surprising. However, the overall pattern was somewhat less complicated than we had originally expected. The outcome is a faster rate of reaction than predicted by simple additivity. The result can be understood in terms of the contrasting hydration properties of hydrophilic salts and hydrophobic alcohols. The added salts moderate the hydrophobic stabilisation of the initial state of the ester, thus increasing the rate of spontaneous hydrolysis.

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