

Group Contributions to Cosphere–Cosphere Interaction Parameters: Ester Hydrolysis in Aqueous Solutions containing Carboxamides

Jan B. F. N. Engberts,^a Rene Kerstholt^a and Michael J. Blandamer^b

^a Department of Organic Chemistry, University of Groningen, Nijenborgh 16, 9747 AG Groningen, The Netherlands

^b Department of Chemistry, University of Leicester, Leicester LE1 7RH, UK

Rate constants for the hydrolysis of *p*-methoxyphenyl dichloroethanoate in dilute aqueous solutions of carboxamides can be quantitatively accounted for using cosphere interaction parameters $G(c)$ which are linear functions of the number of methylene groups in an added carboxamide.

Rate constants for reactions in aqueous solutions are markedly sensitive to the nature and molality of added solute. In attempting to quantify this sensitivity, we expressed the effect of added solute on activity coefficients of both initial and transition states in aqueous solutions using Gibbs energy pairwise solute–solute interaction parameters.^{1,2} The latter can be re-expressed in terms of group interaction parameters using the method described by Savage and Wood;³ *i.e.* the Savage–Wood Additivity of Groups (SWAG) method. Nevertheless reservations can be expressed⁴ concerning the validity of the approach. We report below a convincing example of the success of this analysis based on the effects of added carboxamides on the pseudo-first-order rate constant for the water-catalysed ester hydrolysis of *p*-methoxyphenyl dichloroethanoate in aqueous solutions.^{5,6}

This acyl-activated ester undergoes spontaneous hydrolysis in aqueous solutions, the pseudo-first-order rate constant being independent of pH in weakly acidic solutions. The reaction proceeds *via* rate-limiting water catalysed nucleophilic attack of water at the ester carbonyl group.⁶ The rate constants were measured spectrophotometrically at 298 K by following the decrease in absorbance with time at 288 nm for at least four half-lives. The 75–100 absorbance-time data points conformed to a first-order process, the rate constant being reproducible to within 1%. Rate constants k were measured as a function of the molality m_c of added carboxamide. The data were fitted to eqn. (1) where $G(c)$ is the kinetic interaction parameter expressed in J kg mol^{-2} and where k^0 is the rate constant for reaction in solution when m_c is zero; $m^0 = 1 \text{ mol kg}^{-1}$.

$$\ln(k/k^0) = (2/R \cdot T) \cdot G(c) \cdot (m_c/m^0) \quad (1)$$

We used^{1,2} in the equation for $\ln(k/k^0)$ a further term which

includes the practical osmotic coefficient. Thus, $G(c)$ describes cosphere interactions^{1,2} between added carboxamide and both initial and transition state. Kinetic data were obtained for nine different carboxamides in the concentration range, $0 \leq m_c < 1.2 \text{ mol kg}^{-1}$. For each set of carboxamide solutions, plots of $\ln(k/k^0)$ against m_c produced excellent straight lines. Therefore the assumption is valid that interactions of higher order than pairwise are unimportant. The

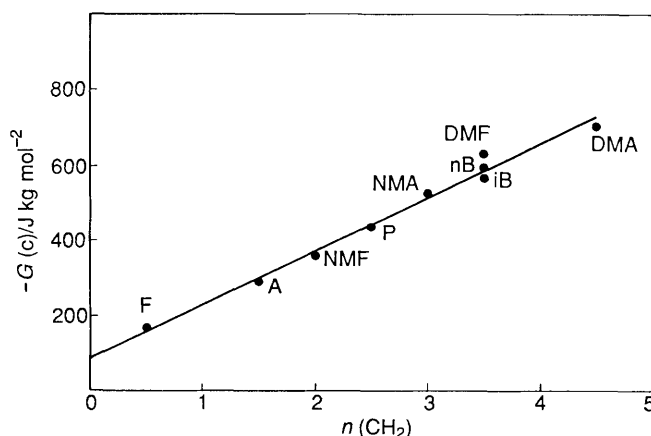


Fig. 1 Dependence of pairwise cosphere–cosphere interaction parameters $G(c)$ on the total number of methylene groups $n(\text{CH}_2)$ in added formamide (F), acetamide (A), *N*-methylformamide (NMF), propionamide (P), *N*-methylacetamide (NMA), *N,N*-dimethylformamide (DMF), *n*-butylamide (nB), *iso*-butylamide (iB) and *N,N*-dimethylacetamide (DMA)

results are summarised in Fig. 1 where we have plotted $G(c)$ against the number of all methylene groups present in the carboxamide solute. We used a scheme³ in which $\text{CH} \equiv 0.5 \times \text{CH}_2$, and $\text{CH}_3 \equiv 1.5 \times \text{CH}_2$. The pattern is, we suggest, excellent supporting evidence for the group interaction model and for its application to understanding kinetic medium effects in dilute aqueous solutions.

The pattern reported here makes an interesting contribution to current discussions concerning the phenomenon of molecular recognition between solutes in aqueous solutions. In thermodynamic terms, the act of molecular recognition between two solute molecules in solution means that the solutions are not thermodynamically ideal. One quantitative description of molecular recognition is in terms of pairwise group interaction parameters. The type of pattern shown in Fig. 1 offers a reference against which to identify those special cases where the interaction between two hydration cospheres is specific to the solutes. Therefore deviations from a simple pattern will signal cases where the molecular recognition is

unique. We explore this point in a full report of these experiments.

We thank the Research Board at the University of Leicester for a travel grant to M. J. B.

Received, 13th May 1991, Com. 1/02245H

References

- 1 W. Blokzijl, J. Jager, J. B. F. N. Engberts and M. J. Blandamer, *J. Am. Chem. Soc.*, 1986, **108**, 6411.
- 2 W. Blokzijl, J. B. F. N. Engberts, J. Jager and M. J. Blandamer, *J. Phys. Chem.*, 1987, **91**, 6022.
- 3 J. J. Savage and R. H. Wood, *J. Solution Chem.*, 1976, **5**, 733.
- 4 F. Franks, *Pure Appl. Chem.*, 1987, **59**, 1189.
- 5 J. F. J. Engbersen and J. B. F. N. Engberts, *J. Am. Chem. Soc.*, 1975, **97**, 1563.
- 6 H. A. J. Holterman and J. B. F. N. Engberts, *J. Org. Chem.*, 1983, **48**, 4025.