Kinetics of the Acid Catalysed Hydrolysis of Formamide in Binary-Aqueous Mixtures

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The kinetics of acid hydrolysis of formamide have been studied in binary aqueous mixtures with acetone, dioxan, 2-propanol and dimethylsulphoxide. The dipolar aprotic and non-hydrogen bond donor solvents like dioxan and acetone have a rate enhancing effect. On the other hand protic solvents like alcohols, which can act both as hydrogen bond donor and acceptor, exert a rate decreasing effect. DMSO, although a dipolar aprotic non-hydrogen bond donor solvent, has a rate decreasing effect possibly due to its strong interaction with hydrogen ions and association with water molecules.

THE kinetics studies in binary-aqueous mixtures have revealed that the effects of non aqueous component on the rate are generally complicated and not amenable to easy explanation in terms of the dielectric properties of the medium[1,2]. It is now recognised that the reorganisation of the solvent surrounding the reactants in the activation process, has a profound influence on the reaction rates. The addition of the cosolvent influences such a reorganisation and it cannot be treated as a mere diluent of water modifying its dielectric properties only[1,2]. Blandamer and Burgess[1] have discussed the interrelation of thermodynamic and structural properties of binary aqueous mixtures and the kinetic rate effects. In order to probe into such an interrelation, it was decided to study the acid hydrolysis of formamide in diverse solvents such as dioxan, acetone, dimethylsulphoxide (DMSO) and 2-propanol. Previously, this reaction has been studied in alkanols[8,4] and in dioxan[5].

In this study an attempt has been made to compare and correlate the kinetic effects of various solvents on the rate with their properties.

Experimental

Formamide (Koch-Light, A.R.), 1,4-Dioxan (Merck, extra pure), acetone (B.D.H., AnalaR),

dimethylsulphoxide (Reidel, prosynth) and 2-propanol (S. Merck, L.R.) were used. All other chemicals were of reagent grade. The experiments were conducted in stoppered conical flasks immersed in water-bath at a desired temperature ($\pm 0.1°$). The reaction was initiated by mixing temperature equilibrated solution of formamide with temperature equilibrated mixture of hydrochloric acid and other chemicals. Aliquots were withdrawn from the reaction mixture after suitable intervals of time and analysed for ammonium ions, one of the reaction products, by formol titration method[6]. The duplicate rate measurements were reproducible within $\pm 5\%$.

Results

For studying the solvent effect, acetone, dioxan, DMSO and 2-propanol were used as cosolvent. The kinetics were studied by varying the percentage of nonaqueous cosolvent from 10 to 80% in binary-aqueous mixtures. The concentration of formamide and HCl were held constant at $0.5M$ each. The second order rate constants, k_2, were obtained using appropriate integrated rate equation in accordance with the rate law,

$$\text{Rate} = k_2 \, [\text{HCONH}_2] \, [\text{H}^+] \qquad (1)$$

The results are given in Table 1.

TABLE 1—SECOND ORDER RATE CONSTANTS (k_2, $M^{-1}\text{SEC}^{-1}$) FOR ACID HYDROLYSIS OF FORMAMIDE IN DIFFERENT AQUEOUS MIXTURES

| Dioxan (40°)		Acetone (40°)		DMSO (40°)		2-Propanol (30°)	
% (v/v)	$10^4 k_2$	% (v/v)	$10^4 k_2$	% (v/v)	$10^4 k_2$	% (v/v)	$10^4 k_2$
0	6.9	0	6.9	0	6.9	0	2.70
20	6.8	20	6.8	20	6.5	10	2.42
40	6.8	40	6.7	40	6.1	15	2.25
60	7.5	50	6.8	60	4.3	20	2.25
80	12.3	60	7.1	80	2.15	30	2.00
		80	11.8			40	1.55
						50	1.40
						60	1.30
						80	1.22

A perusal of the kinetics results shows that in case of acetone and dioxan increasing amount of these solvents upto 40 - 50% in the aqueous mixtures had no effect on the rate. Thereafter the rate increases sharply. Earlier workers[4] have noted a slightly larger decrease in rate in dioxan-water mixtures followed by increase in rate above 50% dioxan-water compositions. The small decrease observed in the present study in the 0-50% range in both solvents is well within the experimental uncertainty of the present rate measurements and therefore does not appear to be significant.

In case of DMSO and 2-propanol the rate decreases continuously with the increase of their percentage composition in binary aqueous mixtures. For 2-propanol similar results have been noted by other workers too[3,4].

Discussion

In many cases the study of the solvent effect has been used as a diagonstic tool in deciding between A-1 and A-2 mechanism or in general between dissociative and associative mechanisms[8,11]. It has been argued[9] that the solvent effects are in general small for A-2 mechanisms. A perusal of kinetics results for different solvent systems (Table 1) shows that in all cases the variation in the values of the rate constants is within a factor of 4 although the solvent composition has been varied over a wide range. Similar kinetic behaviour have been noted by other workers also[3,4]. This clearly establishes a small effect of solvent composition on rate and is in conformity with the A-2 mechanism accepted for amide hydrolysis.

The correlation of solvent effect with mechanism is a ticklish problem and is, in general, dominated more by exceptions than rules. This is particularly true of amide hydrolysis because of the following two step mechanism :

$$RCONH_2 + H^+ \rightleftharpoons RCONH_3^+ \quad \cdots (2)$$

$$RCONH_3^+ + H_2O \longrightarrow RCOOH + NH_4^+ \quad \cdots (3)$$
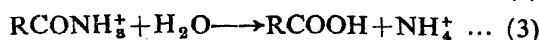
How a particular solvent will affect each step is difficult to discern and what is experimentally observed is the net effect. On the face of it, since the reaction is between an ion and a neutral molecule[12], the rate should increase with the increase in the proportion of the less polar component in the reaction mixture. This is borne out only for acetone and dioxan and that too in the range of 50-80% (v/v) organic component. For others, the rate is found to decrease. For ion-dipole reactions, the present reaction being an example, the plot[12,13] of log k_D and 1/D is expected to be straight line where k_D is the rate constant in a medium of dielectric constant D. Such plots were non-linear for all the solvents studied and in no case a straight line was obtained. When the effect of dielectric constant for all the solvents studied including those by earlier workers, is compared, the dielectric constant as a principal source of solvent effects is ruled out as in all the cases the

dielectric constant of the binary mixtures decreases with increasing organic cosolvent.
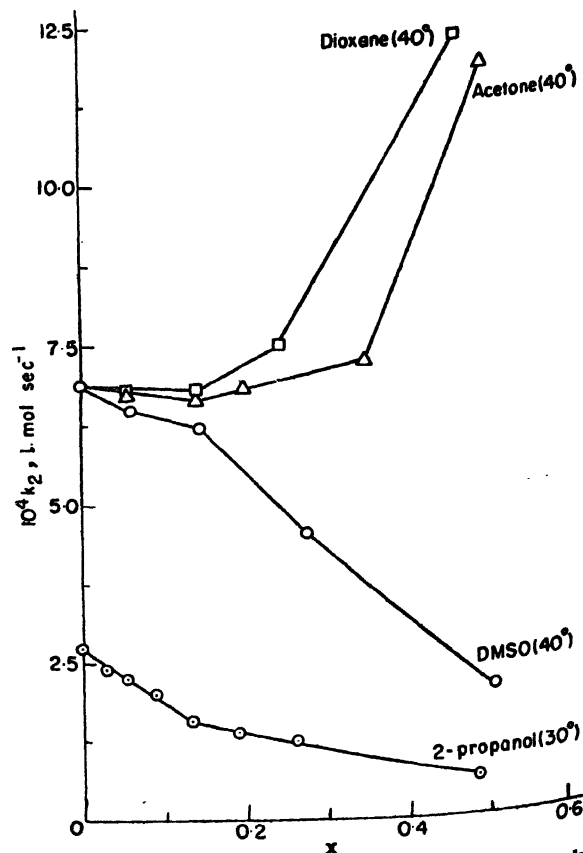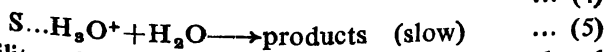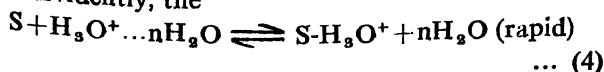

Fig. 1. The variation of second order rate constant, k_2, with the mole fraction, x of organic cosolvent in the acid hydrolysis of formamide.

Fig. 1 shows the variation in rate constant, k_2, with mole fraction, x, of the organic component of the reaction mixture. In case of acetone, dioxan, DMSO and 2-propanol the rate is seen to change anomalously at the x values of 0.30, 0.15, 0.12 and 0.15 respectively. On the basis of thermodynamic functions of state, binary aqueous mixtures have been classified as typically aqueous (TA) and typically non-aqueous (TNA)[1]. TA mixtures are characterised by entropy controlled mixing while in TNA mixtures by enthalpy controlled mixing. In TA mixtures, e.g., acetone-water, alcohol-water etc., as the mole fraction of cosolvent is increased it exerts a water structure forming action, the solvent co-spheres around each solute starts overlapping mutually enhancing water-water interactions. As more cosolvent is added and as soon as the mole fraction exceeds a particular value, x*, there is insufficient water to maintain a three dimensional hydrogen bonded net work of water molecules and localised attempts to maintain this net work result in concentration fluctuations and the effect is maximal at a particular mole fraction x**. The values of x* and x** are reported[1] to be 0.06 and 0.18 for 2-propanol and 0.06 and 0.35 for acetone at 25°. It has been said that these values provide a useful

sign post in effects on kinetic data and they are expected to undergo an anomalous change in these x-ranges. In conformity with the predicted kinetic rate effects the mole fractions (Fig. 1) at which the rates in different media change abruptly coincide remarkably with x* and x** values[1].

The values for the variation of k_2 with mole fraction for DMSO fall on two straight lines. One line lies in the x range of 0 to 0.15 and the other in the range of 0.15 to 0.5, the decrease in rate with increase of x being sharper in the second range. It is interesting to point out that the analysis of kinetics results of the hydrolysis of acetals in DMSO-water mixtures has shown[1,14] that the kinetic behaviour is different in the ranges $0 < x < 0.3$ and $0.3 < x < 0.45$. This is fairly in agreement with the observations made in the present work.

The acid hydrolysis of amides is assumed to involve the hydrogen bond equilibrium as in (4) and (5). Evidently, the

$$S + H_3O^+ ... nH_2O \rightleftharpoons S-H_3O^+ + nH_2O \text{ (rapid)}$$
$$... (4)$$

$$S...H_3O^+ + H_2O \longrightarrow \text{products (slow)} \quad ... (5)$$

ability of a solvent to partake in hydrogen bond formation is likely to influence the rate pattern in binary aqueous mixtures. DMSO and alcohols both are able to form strong hydrogen bonds but the basic difference between them is that while the former is only a hydrogen bond acceptor, the latter acts as donor and acceptor both and therefore the rate effects in the binary mixtures containing alcohols are expected to be more complicated. Indeed the rate constants for the acid hydrolysis of formamide pass through a minimum as the percentage of ethanol, 1-propanol and 2-methyl, 2-propanol is increased[3,4]. 2-Propanol appears to be an exception to this trend as neither we nor earlier workers[3,4] found any minimum in its rate pattern. Based on the fact that a large amount of heat is evolved when DMSO and water are mixed and that the viscosity isotherm passes through a maximum, it is believed that there is a strong association between water and DMSO due to hydrogen bonding[17]. It is known that the amount of free water decreases as the mole fraction of DMSO increases. In fact in the region $0.3 < x < 0.45$, the properties of the system are dominated by an associated species, $H_2O : DMSO$ (2 : 1). In the present work it is this region in which the DMSO has a severe rate decreasing effect. Thus the effect of increasing DMSO in part may be due to decrease in free water concentration necessary for participation in step (2). The effect of DMSO can be explained in one more way. It is known that its basicity is comparable to that of water, and HCl has been found to be fully ionised in it[18,19]. Dehn, Gutman, Kirch and Schober[19] have shown that proton is more strongly bound to DMSO than water. It is thus possible that by tucking away hydrogen ions, DMSO can bring out the decrease in rate by shifting the equilibrium step (2) to the left. This also follows from the results of Tomilla and Musto[17] who found DMSO to decrease the protonation of certain indicators.

Dioxan and acetone both are hydrogen bond acceptor, the former being stronger than the latter. However, in one respect, dioxan is different from alcohols and DMSO. While the latter solvents exert a water-water structure forming action, the former is reported to be structure breaking[1]. This important difference in property may be a reason for rate enhancing effect of dioxan in the acid hydrolysis of amides. In line with the results of the present study, the dioxan and acetone are reported to increase the rate of the acid hydrolysis of γ-hydroxybutyeramide also[15].

The results obtained in the present work can be explained using another approach also. Using phenomenon of solvation of reactants and transition state, Pocker[16,20] has rationalised that the rate should increase with the decrease in polarity of solvent. On this basis, the rate should increase in acetone and dioxan mixtures as is found in the present study. For ion-dipolar molecule reactions the rate is predicted to increase from protic solvents like water and alcohols to dipolar aprotic solvents like dioxan and acetone[16]. This is based on the relative solvating power of two media, the protic solvents being more solvating than aprotic ones[16]. Several examples of reactions of this charge type are known[16] in which the rate increases with decrease in the solvating power of the medium because the solvation energy of the smaller reactant ion, as in steps (2) and (3), is larger than the larger transition state ion causing an increase in the energy of activation in the stronger solvating media and hence the slower reaction rate.

In summary, the following conclusions may be drawn. The dipolar aprotic and non hydrogen bond donor solvents like dioxan and acetone increase the rate while protic solvents like alcohols decrease the rate. DMSO, although a dipolar aprotic solvent, decreases the rate and this could be due to its strong interaction with H^+ and association with water molecules.

References

1. M. J. BLANDAMER and J. BURGESS, Chem. Soc. Rev., 1975, 4, 55.
2. E. S. AMIS and J. P. HINTON, "Solvent Effects on Chemical Phenomenon", Vol. I, Academic Press, 1973.
3. I. M. SIDAAHMED, S. M. SALEUR, F. M. ABDEL HALIM, J. Indian Chem. Soc., 1980, 57, 624.
4. M. M. ELSEMONGY and H. M. ABU ELNADER, J. Indian Chem. Soc., 1977, 54, 1055.
5. S. MITTAL, K. S. GUPTA and Y. K. GUPTA, Indian J. Chem., 1977, 15A, 827; P. B. HAUK, "Practical Physiological Chemistry" P. BLAKISTON, Philadelphia, 1920, p. 525.
6. J. BURGESS, J. Chem. Soc. Dalton Trans., 1973, 825.
7. E. GRUNWALD and S. WINSTEIN, J. Amer. Chem. Soc., 1948, 70, 846; P. R. WELLS, "Linear Free Energy Relationships", Academic Press, London, 1968, Chap. 4.
8. J. BURGESS, P. M. MEKHAIL and E. ROY GORDNER, J. Chem. Soc. Dalton Trans., 1973, 1335.
9. R. W. HAY, C. R. CLARK and J. A. G. EDMONDS, J. Chem. Soc. Dalton Trans., 1974, 9.
10. C. A. BUNTON and B. N. HENDY, J. Chem. Soc., 1963, 3130.
11. R. HUDSON and B. SAVILLE, J. Chem. Soc., 1955, 4114.

12. A. A. FROST and R. G. PEARSON, "Kinetics and Mechanism", Wiley, 1961, p. 149.

13. E. S. AMIS and J. P. HINTON, "Solvent Effects on Chemical Phenomenon", Vol. I, Academic Press, 1973, p. 254.

14. R. K. WOLFORD, J. Phys. Chem., 1964, 68, 3392.

15. T. YAMANA, A. TSUJI and Y. MIZUKAMI, Chem. Pharm. Bull., 1972, 20, 2528.

16. E. S. AMIS and J. P. HINTON, "Solvent Effects on Chemical Phenomenon", Vol. I, Academic Press, 1973, p. 302.

17. E. TOMILLA and M. L. MURTO, Acta Chem. Scand., 1963, 17, 1947 ; and references therein.

18. I. M. KOLTHOFF and T. B. REDDY, Inorg. Chem., 1962, 1, 189.

19. H. DEHN, V. GUTMAN, H. KIRCH and G. SCHOBER, Monatsh. Chem., 1962, 93, 1439.