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SOLVENT EFFECTS ON THE KINETICS OF THE ALKALINE CATALYSED HYDROLYSIS OF CYANOACETAMIDE

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The rate of the alkaline catalysed hydrolysis of cyanoacetamide was investigated in the presence of ethanol and ethylene glycol up to 60 wt % in the temperature range 25 to 45+0.1°C The reaction rate decreased with the progressive addition of ethanol, while in case of ethylene glycol decreased up to 40 wt % then increased. The isocomposition and isodielectric energies of activation and the thermodynamic parameters of activation were calculated and discussed in terms of solvent effects. The influence of the dielectric constant of the solvent mixture on the reaction rate was discussed. A mechanism was proposed to account for the effect of the solvent on the reaction rate.

INTRODUCTION

The problem of amide hydrolysis in mixed solvents has been discussed by many authors, and was looked at from different points of view(1,2). The rates of hydrolysis of formamide(3), acetamide(4) and propionamide(5,6) were studied in different media. The rates of acidic and basic hydrolysis were found to increase with increasing dielectric constant of the medium. A general equation for the variation of specific rate constant with dielectric constant has been proposed(7,8). However, few studies have been done on the hydrolysis of cyanoacetamide. In previous work we have studied the effect of methanol(9) and n-propanol nol(10) on the reaction kinetics. In the present work, the studies have been extended to other two- mono- and dihydric alcohols in order to investigate the effect of solvents on the kinetics and mechanism of the hydrolysis of cyanoacetamide.

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EXPERIMENTAL

The general experimental procedure was similar to that described earlier(3). Pure reagents, cyanoacetamide, ethanol, ethylene glycol and sodium hydroxide (E Merck) were used. Deionized water was used throughout. The initial concentrations of both amide and sodium hydroxide were 0.05 M throughout the work and the rate of hydrolysis was measured in the 25–45 ± 0.1°C range. All solutions were allowed to equilibrate at the desired temperature before mixing. Rate constants represent the mean of three independent determinations. The values were generally reproducible within ± 1 %. The values of the dielectric constant were obtained by interpolation from large-scale plots based upon Akerlof's data(11).

RESULTS AND DISCUSSION

The reaction is first order with respect to the amide and to the base, thus the hydrolysis reaction follows an overall second order kinetics. Accordingly, for each individual solvent composition, the plot of $\frac{x}{a-x}$ versus time is a line passing through the origin. The second order rate constants were calculated from the slopes of these linear plots using least-squares method, and are listed in Table I. It is evident from these

Table 1. Second order rate constants ($10^4 k_2$, $dm^{-3}\ mol^{-1}\ s^{-1}$) and isocomposition activation energies (Ec, $KJmol^{-1}$) for the alkaline hydrolysis of cyanoacetamide in alcohol-water mixtures.

Alcohol wt %	25°C	30°C	35°C	40°C	45°C	Ec
	Ethanol-water					
0	16.98	25.12	35.48	52.47	72.44	58.43
10	13.49	19.95	28.84	41.68	62.26	60.80
20	10.47	15.49	22.91	33.67	52.48	65.33
30	8.51	12.59	19.06	28.18	44.69	68.97
40	7.24	10.96	16.60	25.11	39.15	70.78
50	5.62	8.91	13.48	20.89	33.88	74.41
60	4.07	7.08	10.96	17.38	30.20	77.13
	Ethylene glycol-water					
10	13.18	19.50	28.51	42.65	61.66	60.62
20	9.77	15.14	22.38	34.67	52.48	65.06
30	7.24	12.88	18.62	28.84	44.67	70.27
40	5.37	8.91	14.45	22.91	37.15	75.41
50	6.31	10.23	16.60	26.30	41.68	73.18
60	8.51	11.48	19.95	31.62	47.86	68.01

results that the rate of hydrolysis decreases with increasing ethanol content, while it decreases with ethylene glycol amount up to 40 wt % and then increases slightly with progressive addition of ethylene glycol to the medium. This variation of the reaction rate constant with the solvent composition at constant base concentration may be attributed to the changes in the solvent system through the equilibrium:

$$(H_2O)_3OH^- + nS \rightleftarrows nH_2O + (H_2O)_{3-n} + SnOH^- \qquad (1)$$

This equilibrium involves substitution of water by the organic solvent molecule in the ion clusters by multi-step solvation mechanism(12). Therefore, the number of free water molecules increases on progressive addition of either ethanol or ethylene glycol; and this plays an important role in the dependence of reaction rate on the solvent composition. The dependence of reaction rate on water concentration was illustrated by a linear relation between log k_2 and log Cw shown in Figure 1. The slopes of these lines, as generally known, represent the number of water molecules involved in the formation of the activated complex. Thus, the rate of the reaction is proportional to the concentration of water in agreement with the expected bimolecular mechanism.

It has been reported that when sodium hydroxide is dissolved in ethanol, the solutions mainly contain ethoxide ions rather than hydroxide ions(13). The conclusion was that the basicity of ethoxide ion is less than that of hydroxide ions. Moreover, stabilization of ethoxide ion may occur by hyperconjugative resonance. Thus, it would not be surprising in this case that the rate constant decreases continuously by the successive addition of ethanol to the reaction medium although the dielectric constant of the medium decreases. On the other hand, the anion of ethylene glycol may be stabilized by intermolecular hydrogen bonding of an unreacted hydroxyl group and the alkoxide oxygen atoms(14); the activity of such anion may be enhanced at the lower dielectric constant region, since the charge is somewhat dispersed through this hydrogen bonding.

The hydrolysis reaction was carried out at different temperatures in the 25–60 ± 0.1°C range in various alcohol-water solvent mixtures. The isocomposition activation energies were calculated from the slopes of the linear Arrhenius plots shown in Figure 2 and are listed also in Table 1. It is noteworthy that while the rate constant decreases the activation energy increases with progressive addition of either of the two alcohols to the reaction medium. This increase in activation energy can

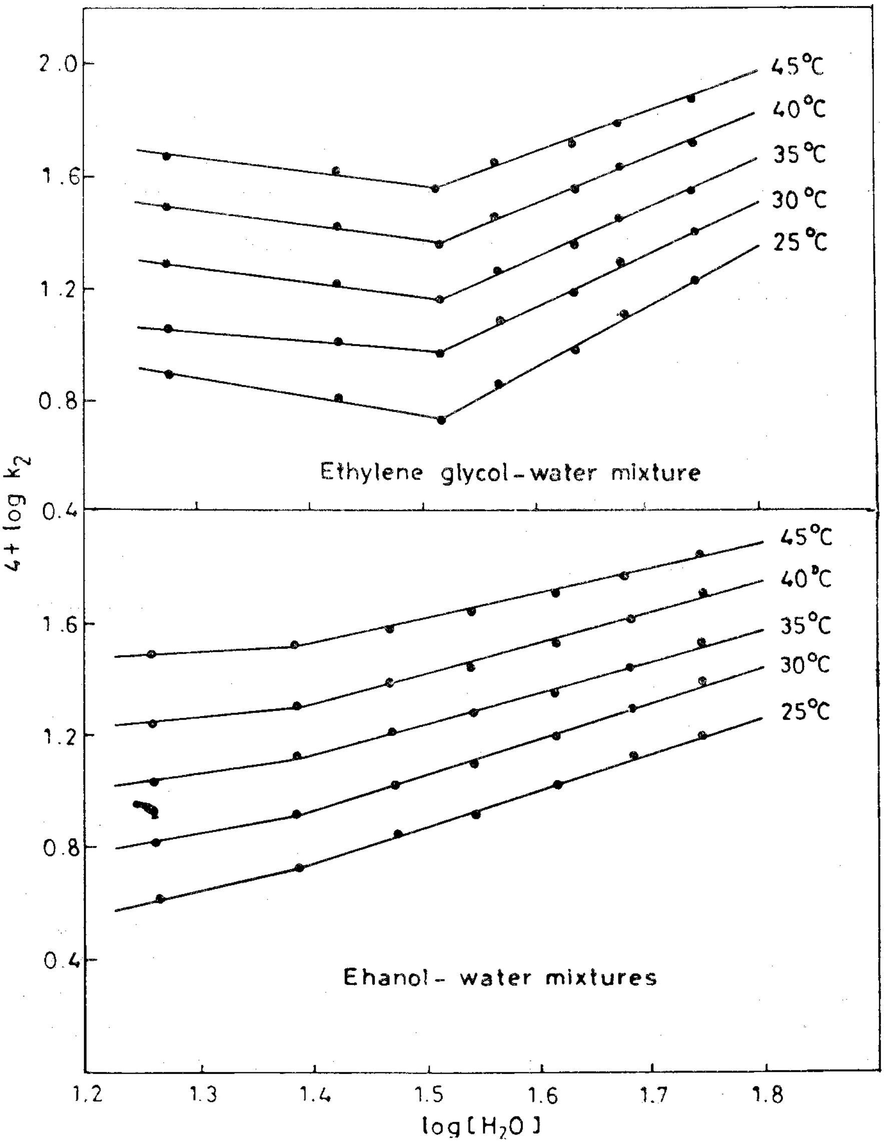

Fig. 1. Variation of rate constant with water concentration.

be attributed to the solvation of the reactants to a greater extent than that of the activated complex(3,4). However, the enthalpy ($\triangle H^*$) and the entropy ($\triangle S^*$) as of activation could be more sensitive indicators

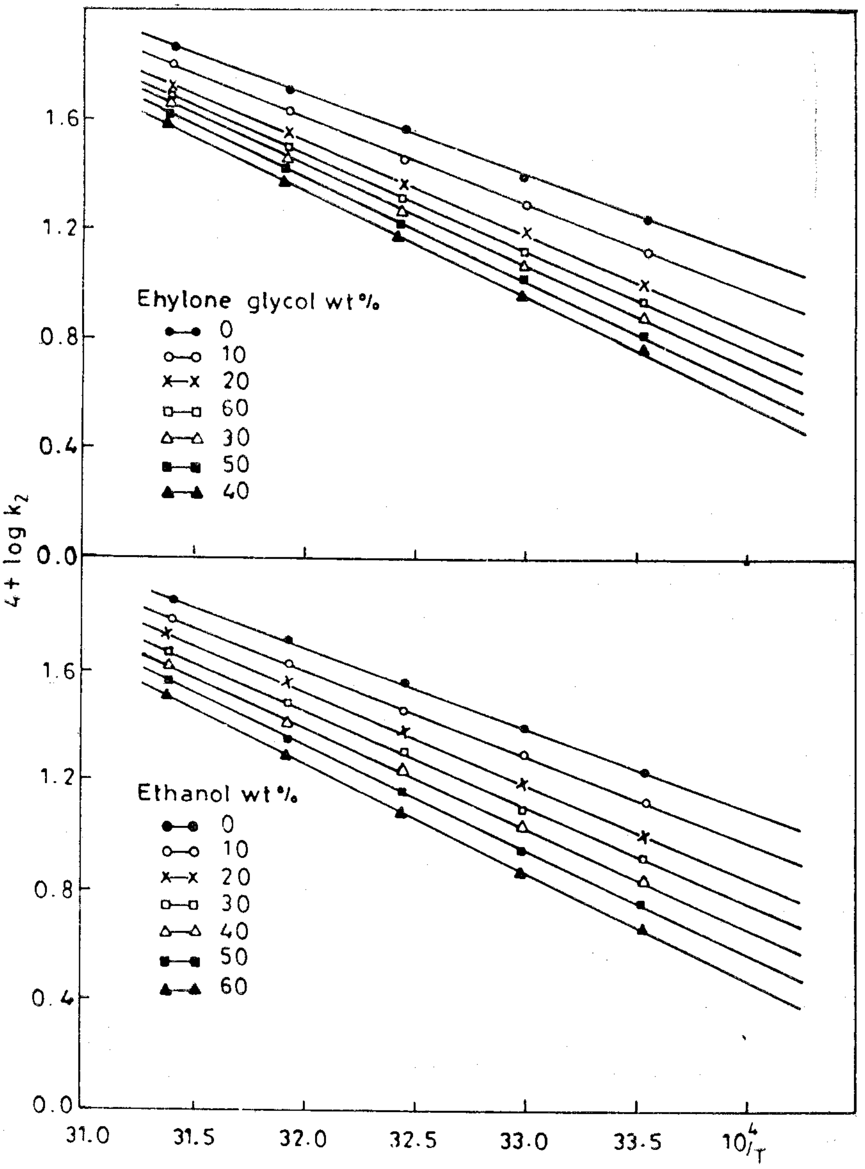

Fig. 2. Arrhenius plots in different solvent mixtures.

of the effects of solvent structure than the rate constant directly⁽¹⁵⁾. The activation parameters were calculated and are listed in Table II.

The enthalpy of activation varies successively with increasing either ethanol or ethylene glycol content in the solvent mixture. This be-

Table 2. Thermodynamic parameters of activation at 25°C ($\triangle H^*$ and $\triangle G^*$ in KJ mol^{-1} and $\triangle S^*$ in J mol^{-1} K^{-1}).

Alcohol wt %	Ethanol-water			Ethylene glycol-water		
	$\triangle H^*$	$\triangle G^*$	$-\triangle S^*$	$\triangle H^*$	$\triangle G^*$	$-\triangle S^*$
0	55.95	88.87	110.4	55.95	88.87	110.4
10	58.32	89.45	104.4	58.14	89.50	105.2
20	62.85	90.07	91.3	62.58	90.24	92.7
30	64.69	90.59	86.9	67.79	90.98	77.8
40	68.83	90.99	74.3	72.93	91.73	63.1
50	71.93	91.62	66.2	70.70	91.33	69.2
60	74.65	92.41	59.6	65.53	90.59	84.1

haviour may be a direct consequence of the variation of isocomposition activation energy with the dielectric constant. The free energy of activation, $\triangle G^*$, increases gradually with increasing alcohol content in both cases and decreases in case of ethylene glycol passing through a maximum at 40 wt %. According to the theory of absolute reaction rates, an increase in $\triangle G^*$ is an indication of the solvation phenomena. This agrees with the observed increase in the energy of activation in the same direction. Therefore, solvation is expected to be more pronounced in presence of the alcohols. The enthalpy of activation varies with increasing the alcohol content in the solvent mixture in a non-linear manner. The non-linear behaviour is a criterion of specific solvation(16).

The principle aim of this investigation is the study of the influence of the dielectric constant of the medium on the reaction rate and mechanism. This influence can be expected on the basis of the following equation(7) which predicts a linear relationship between the rate constant and the dielectric constant:

$$k = k' e^{\alpha}(D-1) \tag{2}$$

where k is the rate constant, k′ is its value at D = 1 and α is a constant. Linear plots of log k_2 versus D were obtained as shown in Figure 3. It was observed that the rate constant increases with increasing dielectric constant of the solvent mixture. This may be ascribed to the formation of a polar activated transition state.

The experimental activation energies involve a highly mixed dependence of the rate constant on the temperature and on the dielectric constant of the medium. In order to obtain a more precise treatment of the results, the temperature dependence of the dielectric constant should be eliminated. This is achieved by calculating the isodielectric activation energies, E_d, from the corresponding rate constants in isodielectric solutions. The latter obtained by interpolation at chosen values of dielectric constant, from the plots of log k_2 versus D shown in Figure 3. The values of E_d then were obtained from Arrhenius plots, and are listed in Table III.

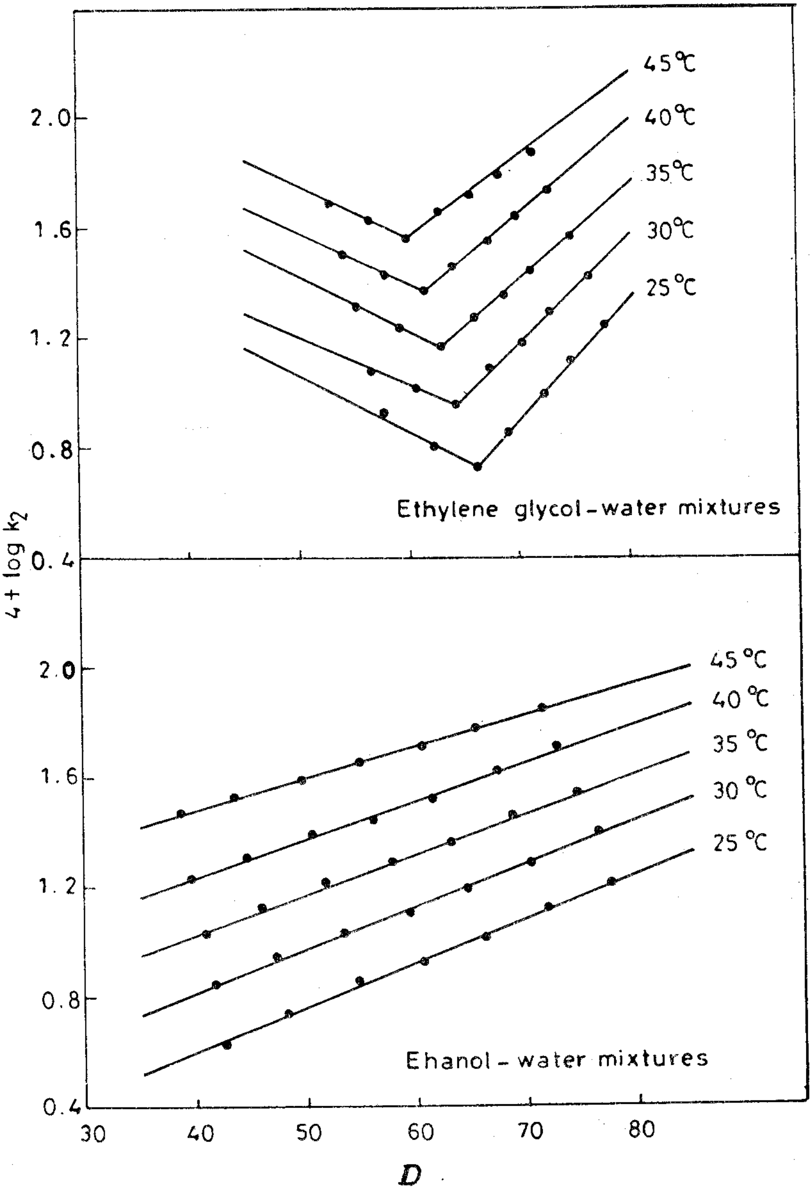

Fig. 3. Effect of dielectric constant on reaction rate.

Table 3. Interpolated values of rate constant at constant dielectric constant ($10^4 k_d$, dm^{-3} mol^{-1} s^{-1}) and isodielectric activation energy (Ed, KJ mol^{-1}).

D	$10^4 k_d$					E_d
	25°C	30°C	35°C	40°C	45°C	
	Ethanol-water					
55	6.92	10.72	17.38	27.54	44.66	74.67
60	8.13	12.88	20.41	31.62	50.12	72.76
65	10.23	15.49	23.99	37.15	57.54	70.84
70	12.02	19.05	28.84	43.65	66.07	67.14
75	14.45	22.91	34.67	52.48	75.86	64.14
	Ethylene glycol-water					
55	12.88	12.59	20.41	30.19	43.65	61.27
60	7.59	10.47	15.85	23.98	35.48	63.19
65	5.62	9.12	16.56	30.90	50.12	91.11
70	6.92	14.45	25.12	43.65	70.70	89.99
75	8.91	23.44	38.02	66.07	97.72	82.33

From an electrostatic point of view, a rate decrease might be expected because of destabilisation of the polar transition state when the bulk dielectric constant is lowered by successive addition of alcohol(15). Since the higher polar transition state is more strongly solvated relative to less polar ground state, it is expected that as the solvent polarity decreases, the reaction rate decreases.

The proposed mechanism for the alkaline hydrolysis of cyanoacetamide should account satisfactorily for the role and for the effect of the solvent on the reaction rate. It was noticed that the successive addition of either of the alcohols alters the rate without influencing the mechanism and so the mechanism is the same for the different solvent composition. A bimolecular mechanism was proposed(10). This mechanism involves a fast pre-equilibrium nucleophilic attack of the solvated hydroxyl ions on the amide molecule as follows:

$$A + S\,OH^- + H_2O \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} T^- + S(\text{fast}) \qquad (3)$$

$$T^- + H_2O \xrightarrow{k_2} \text{Products (slow)} \qquad (4)$$

where A is the amide molecule, S is the solvent molecule and T^- stands for the solvated transition state. The cyano group, which acts as electron withdrawing substituent, facilitates the nucleophilic attack of OH^-

on the carbonyl group. Activation energies and activation entropies give evidences supporting the validity of this mechanism.

Assuming that steady state concentration is attained in the mixed solvent for the intermediate T, the rate equation can be derived as follow:

$$\begin{aligned} k_1 [A] [SOH^-] [H_2O] &= k_{-1} [T^-] [S] + k_2 [T^-] [H_2O] \\ &= [T^-] \{k_{-1} [S] + k_2 [H_2O]\} \qquad (5) \end{aligned}$$

then, we have

$$[T] = \frac{k_1 [A] [SOH^-] [H_2O]}{k_{-1} [S] + k_2 [H_2O]} \qquad (6)$$

Since the rate $= k_2 [T^-] [H_2O]$ (7)

substitution for $[T^-]$ from equation (6) in equation (7) we have

$$\begin{aligned} \text{Rate} &= \frac{k_1 k_2 [A] [SOH^-] [H_2O]^2}{k_{-1} [S] + k_2 [H_2O]} \\ &= \frac{k_1 k_2 [A] [SOH^-] [H_2O]^2}{k_{-1} [S] + k_2 [H_2O]} \qquad (8) \end{aligned}$$

since $k_2 << k_{-1}$, k_2 can be neglected in the denominator of equation (8), thus

$$\text{Rate} = \frac{k_1 k_2 [A] [SOH^-] [H_2O]^2}{k_{-1} [S]} \qquad (9)$$

Accordingly, the rate varies directly with water concentration and varies inversely with the solvent concentration, and so, the rate increases by increasing water concentration and decreasing solvent concentration.

REFERENCES

[1] STREITWIESER, A.Jr., "Solvolytic Displacement Reactions", McGraw-Hill, New York; (1962).

[2] AMIS, E.S., "Solvent Effects on Reaction Rates and Mechanism", Academic Press, New York (1966).

[3] ELSEMONGY, M.M., ABU EL NADER, H.M., J. Ind. Chem. Soc., 54, 1055 (1977); 55, 60 (1978).

[4] ELSEMONGY, M.M., Abu ELAMAYEM, M.S.; MOUSSA, M.N.H., Z. Physik, Chem. Neue Folge, 94, 69 (1975); 95, 215 (1975).

[5] ABU EL-NADER, H.M., MOSTAFA, M.R., Rev. Roum. Chim., 33, 7 (1988).

[6] ELSEMONGY, M.M., AMIRA, M.F., AHMED, A.M., Ind. J. Chem., 20A, 802 (1981).

[7] ELSEMONGY, M.M., Z. Physik, Chem. Neue Folge, 84, 294 (1973).

[8] ELSEMONGY, M.M., AMIRA M.F., J. Ind. Chem. Soc., 37, 506 (1980).

[9] ABU EL-NADER, H.M., MOUSSA, M.N.H., MOSTAFA, M.R.,Ind. Chem.,26A, 868 (1987).

[10] MOSTAFA, M.R., Abu EL-NADER H.M., Egypt. J. Chem., 31 (6), 673 (1988).

[11] AKERLOF, C., J. Amer. Chem. Soc., 54, 4125 (1932).

[12] KONDO, Y., TOKURA, N., Bull. Chem. Soc., Jap., 45, 818 (1972).

[13] CALDIN, E.F., LONG, G., J. Chem. Soc., 3737 (1954).

[14] GOULD, E.S., "Mechanism and Structure in Organic Chemistry", Holt, Rinehart and Winston, Inc. New York (1959).

[15] OAKENFULL, D.G., Aust. J. Chem., 27, 1423 (1974).

[16] HUDSON, R.F., Saville, B., J. Chem. Soc., 4114 (1955).