

ACID HYDROLYSIS OF PHENYL ACETAMIDE IN MIXED SOLVENT

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The kinetics of acid hydrolysis of phenyl acetamide has been studied in alcohol-water and dioxane-water in the ratio 50:50 at different temperatures (35–60°C). Since the acid hydrolysis is somewhat slow, high concentration of acid i.e. 3N HCl has been used in every experiment. In all cases the reaction was found to follow the first order kinetics. However, a break was noticed in the plot of $\log(a-x)$ vs. time giving two distinct straight lines. Probable mechanism of hydrolysis has been discussed. The energy of activation and the frequency factor were calculated in the two different solvent systems.

Though the acid and base hydrolysis of both aliphatic and aromatic amides has been investigated, the kinetics of hydrolysis of an amide with benzene ring substituted at α -position to carbonyl carbon atom has not been fully investigated. In the hydrolysis of phenyl acetamide in acid medium, Ali¹ observed the phenomenon of maximum hydrolysis rate, as has been found in the case of other amides.²⁻⁵ Like other aliphatic amides, phenyl acetamide also follows first order rate equation. Ali indicated the existence of a break in the line of $\log(a-x)$ vs. time, suggesting a change in the mechanism at the later stage of hydrolysis.

In the present investigations the existence of a break when the hydrolysis reaction is carried out in mixed solvents, alcohol-water and dioxane-water, in the temperature range of 35° to 60°C has been established.

Experimental

Phenyl acetamide, prepared from phenylacetic acid, was repeatedly recrystallized to obtain a product with a m.p. of 157°C.

The hydrolysis reaction was carried out at 40°, 50° and 55°C in dioxane-water, and at 35° 45° and 60°C in alcohol-water in the ratio 50:50, keeping the acid concentration (3N HCl) and amide concentration (0.1M) constant.

Exactly 0.1M solution of phenyl acetamide was prepared. Measured quantity of the reaction mixture was then transferred to Pyrex test tubes. The attachment of the reaction tube to the holder and the immersion of the same in a constant temperature bath took about 20 minutes. The time required for filling process was maintained in all the experiments.

The reaction tube was removed at suitable intervals, and the contents analysed for ammonia. Sorensen's formal titration⁶ method, with essen-

tial modifications, was used for the determination of ammonia. Formaldehyde reacts with ammonium salts in a neutral solution forming hexamethylenetetramine and liberating an equivalent amount of mineral acid which is then titrated with standard base.



Result and Discussion

The reaction was found to be of first order both from $\log(-dc/dt)$ vs. $\log c$ plots as well as from the linear plot of \log (initial slope) against $\log c$.

All the aliphatic amides so far studied²⁻³ have been shown to have first order hydrolysis rate. Our results is quite in harmony with them. All the aromatic amides have been found to follow second order law both in acid and base hydrolysis.⁷⁻⁸

Figures 1-4 show the $\log(a-x)$ vs. time plots in alcohol-water and dioxane-water at different temperatures.

There are breaks in the graphs, the experimental data falling clearly on two straight lines. The extent of hydrolysis at the point of break for different temperatures and in different solvents are given in Table 1.

The breaks occur only after 50% hydrolysis. Such a break has not been reported so far. Our observation can hardly be overlooked since the phenomenon occurs in every experiment, at different temperatures as well as in different solvents. The break in these plots suggests that there are possibly two mechanisms by which the amide hydrolysis takes place. Since similar behaviour is exhibited in both the solvent systems, the same mechanism occurs in both the cases.

The specific rate constant is calculated independently from the slope of both the straight lines. The rate constant of the first straight line is de-

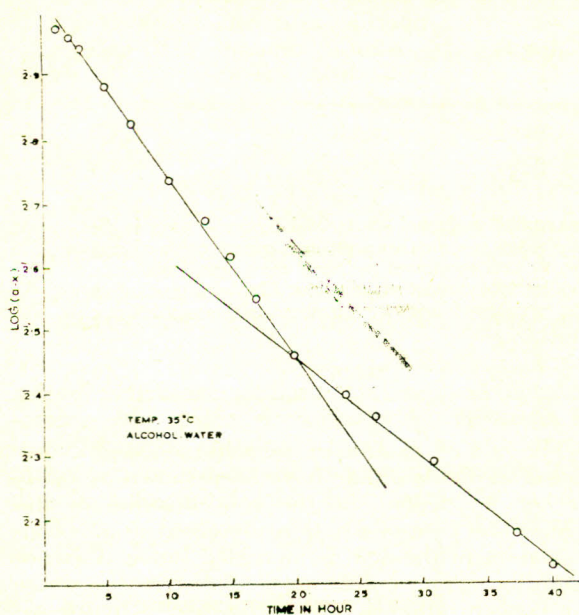


Fig. 1.

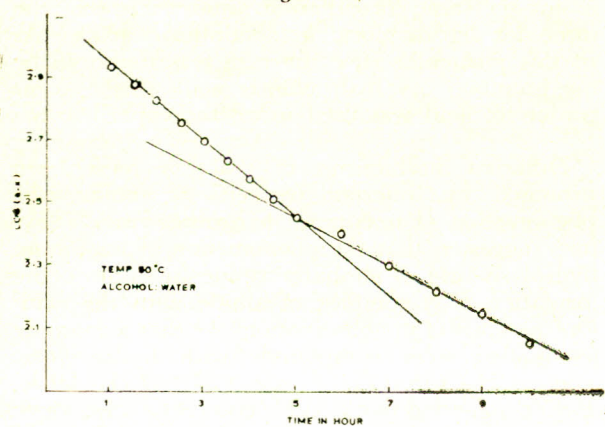


Fig. 2.

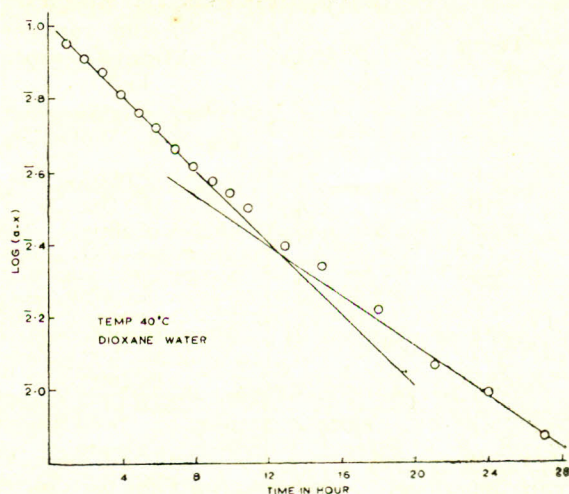


Fig. 3.

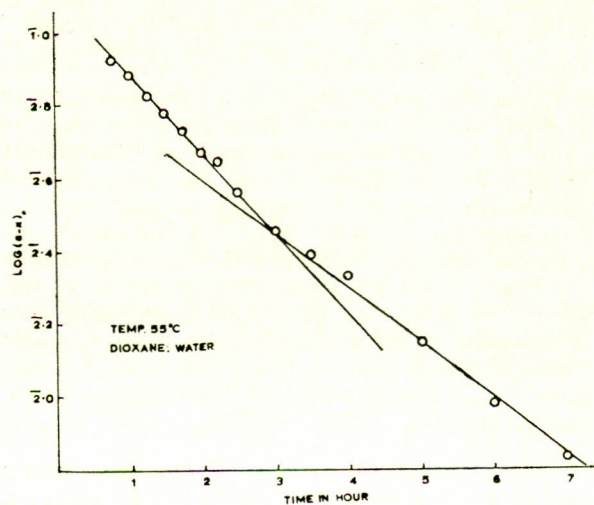


Fig. 4.

signated as K_1 and that of the second line as K_2 . The values of K_1 and K_2 are shown in Table 2.

Values of energy of activation calculated from the slope of $\log K$ vs. $1/T$ plot, in two solvent systems as well as for the two straight lines, are as follows:

Solvent	Specific rate	Activation energy
Alcohol-water system	K_1	19.48 kcals
	K_2	18.60 kcals
Dioxane-water system	K_1	17.42 kcals
	K_2	15.61 kcals

TABLE I

Solvent temp °C	Alcohol-water % hydrolysis at point of break	Solvent temp °C	Dioxane-water % hydrolysis at point of break
35°	71.8	40°	73
45°	53.1	50°	84.8
50°	56.6	55°	67.2
60°	84.5		

TABLE 2

Temp °K	$1/T \times 10^6$	Specific rate constant k_1 time in hr ⁻¹	$\log k_1$	Specific rate constant k_2 time in hr ⁻¹	$\log k_2$
Solvent alcohol-water					
308	3247	0.0665 ₅	$\bar{2}.8231$	0.0389	2.5908
318	3145	0.1562	$\bar{1}.1936$	0.0999 ₅	$\bar{2}.9998$
323	3095	0.2803	$\bar{1}.4477$	0.1667	$\bar{1}.2219$
333	3003	0.7438	$\bar{1}.8715$	0.1843	$\bar{1}.2655$
Solvent dioxane-water					
313	3194	0.1077	$\bar{1}.0322$	0.0878	$\bar{2}.9435$
323	3095	0.2903	$\bar{4}.4628$	0.2054	$\bar{1}.3118$
328	3048	0.4903	$\bar{1}.6905$	0.2534	$\bar{1}.4055$

The frequency factor A is calculated using the equation $\log_e k_1 = \log_e A - (E/RT)$ for two solvent systems at 50°C and only for the first straight line. In case of alcohol-water the value obtained is 1.26×10^{12} litre mole⁻¹ sec⁻¹ and for dioxane-water the value is 5.13×10^{10} litre mole⁻¹ sec⁻¹.

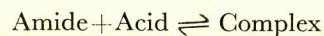
If the energy of activation in the two solvent systems are compared it may be noted that its value is less in dioxane-water than in alcohol-water. The increase of reaction velocity and consequent decrease in energy of activation by changing the solvent from alcohol-water to dioxane-water is presumed to be due to the changing character of solvation. A comparison of the energy of activation of phenyl acetamide with that of some of the aromatic and aliphatic amides from references 7 and 8 shows that phenyl acetamide has a value intermediate between benzamide and acetamide.

Recent investigations have shown that whatever be the true mechanism of hydrolysis, whether it is the old proposition of imino-amino tautomerism or the newest assumption of simultaneous addition of H₃O⁺ and H₂O molecules, the charge on >CO carbon atom is the factor affecting the energy of activation.

The character of CH₃ group is quite different from that of C₆H₅. It has a tendency to lose negative charges shown by its group dipole of +0.4 when substituted in benzene. The charge on >CO carbon atom is, therefore, lower in acetamide and the energy of activation is low. In case of benzamide the >CO carbon atom appears to have developed a large positive charge due to the close proximity of C₆H₅ groups, and the activation energy is increased. From these considerations phenyl acetamide is expected to have an activation energy intermediate between the two. This is borne out by our results.

The rate of reaction of the acid-catalysed hydrolysis of aliphatic amide have been shown by many workers to depend on the concentration of the acid. The rate of reaction increased as the concentration of the acid is increased but it does not go on increasing indefinitely. In every case there is a concentration at which the rate of hydrolysis of the amide is maximum. This concentration is not the same for different amides nor is it the same for hydrochloric and sulphuric acids. As in this particular case the rate was found to be maximum at 3N hydrochloric acid, this concentration of acid was used in all the experiments.

Different mechanisms of reaction have been proposed by different workers to explain the phenomenon of maximum hydrolysis rate. Taylor² suggested that the phenomenon of maximum hydrolysis rate of aliphatic amide was due to the formation of a complex of amide with the acid. On the basis of the observation⁹⁻¹⁰ that acetamide forms two solid compounds with hydrochloric acid (2CH₃CONH₂.HCl and CH₃CONH₂.HCl), Taylor suggested that a stable complex of the above type exists in solution. He postulated the equilibrium



for which the equilibrium constant is expressed as $K = [P\text{Amides}]^2 / [\text{Complex}]$ where P is partial vapour pressure of the acid over the solution.

The existence of a break in the plot of $\log(a-x)$ vs. time giving two distinct straight lines can be explained by the postulation of Taylor. The acid concentration being high (3N) relatively stable complex is formed in solution. At the initial stage of the hydrolysis reaction the free amide undergoes hydrolysis according to the first order rate equation. When a large proportion of the free amide is removed, the rate of breakdown of the complex to give free amide becomes

the rate-determining step in the hydrolysis reaction. If this is a relatively slow process after some time the rate of hydrolysis will diminish, which is in agreement with our present observation.

The possibility of arresting the equilibrium at a low temperature and isolating the intermediate complex is under investigation.

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