Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2012, 4(1):239-245

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Kinetics of Amino Acid Catalyzed Enolisation of Acetophenone

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ABSTRACT

The present investigation deals with the study of kinetics of enolisation of acetophenone in water-Ac-OH binary mixture catalyzed by amino acid. Rate of enolisation of the ketone has been studied in water-Ac-OH binary mixture and it has been briefly compared with the rate using DMF (Dimethyl Formamide), as another solvent, using amino acid as catalysts. Zwitter ion of the amino acid has been found to catalyze the reaction. The reaction followed first order kinetics. The values of Arrhenius parameters for the reaction have been calculated and data obtained confirmed the reaction to be of bimolecular nature. Amino acid has been found to be very effective in the enolisation of ketones. The rate controlling step is the reaction between keto form of ketone and Zwitter ion of amino acid to form a transition state, which decomposes to give enol form of the ketone. Rate of enolisation under present investigation is measured by halogenation. Rate of acetophenone enolisation is enhanced when the medium is changed from protoic to dipolar aprotic solvent.

Keywords: Enolisation, acetophenone, kinetics, zwitter ion, amino acid.

INTRODUCTION

Kinetics of enolisation of ketones has been of great importance in the history of chemistry since it is related with a well known phenomenon of tautomerism [1]. The rates of enolisation of ketones are usually measured by the rates of their halogenations [2], recemization [3] and deuteration [4]. A detailed survey of literature reveals that enolisation kinetics is mainly concentrated to the study of acetophenone and substituted acetophenones [5-13] in acidic and alkaline media.

Since amino acids play an important part of utmost importance in vital processes [14, 15] [14-17] the study of their application in various fields of chemistry is of significance. A large number of workers have reported the acid catalyzed enolisation of aliphatic, aromatic and cyclic ketones [18, 19]. Shilov and Yasnikow have measured for the first time enolisation rate of acetone catalysed by amino acid, glycine [20]. The rate was found to be of first order with respect to acetone and zero order with respect to iodine. The amino acid glycine was found to accelerate the rate of iodination, that is the enolisation of acetone.

The enolisation of acetophenone [21] occurs via tautomerism which is a reversible formation of enol from enolisable ketones. The two structural isomers differ in the relative positions of their atoms and are in rapid equilibrium with each other.

The enolisation could be acid catalysed or base catalysed [22-24] .The amino acids contain two reactive groups, amino and carboxyl group [25] each of which modifies the character of the other that these substances cannot be considered merely as amines and acids. The amino acid molecules exist very largely as an internal salt [26] , which is formed by a shift of the proton from the carboxyl to the amino group. The salt has ionic valancy structure, but the positive and the negative ions are not free to migrate because of their firm union through the carbon atom. Such an internal salt is known as Zwitter ion [27], hybrid ion or dipolar ion which is responsible for the catalytic reaction. Every amino acid has an isoelectric point [28] (a definite pH) at which it fails to migrate under the influence of electric current. For monoamino mono carboxylic acid this value has been found to be six [29]. At this point concentration of the Zwitter ion is the maximum, and so the catalysis will be maximum at this range. Such catalytic activity of the Zwitter ion has also been shown by some other workers [30]. All the four amino acids used under the present investigation, are monoamino monocarboxylic acids viz. Glycine, β alanin, DL alanin and L alanin which are amongst twenty standard amino acids [31] , and the catalytic effect of these on the enolisation kinetics of acetophenone have been studied.

EXPERIMENTAL SECTION

Stock solution of acetophenone was prepared by dissolving it in 100% acetic acid. Aqueous stock solution of amino acids, iodine and hypo were prepared in doubly distilled water. Four Amino acids namely glycine, β alinine, DL alinine and L alinine were used as catalysts. All the chemicals used in the present research were of A.R. grade.

The solutions of iodine (0.006 M) and hypo (0.1M) were standardized before use. Reaction mixtures were prepared by mixing all the reagents except ketone in requisite quantities in standard flasks which were then kept in a thermostat (± 0.03ºC) for about half an hour. The reaction was initiated by the addition of 5ml of 0.1M ketone solution to the flask containing reactants, followed by thorough shaking. Studies were carried out by quenching aliquots (5ml) withdrawn at fixed intervals of time and estimating the residual iodine by titrating it against hypo, using starch as an indicator. This indicated iodine at zero time .Rate of enolisation was studied by iodination and the progress of the reaction was followed by withdrawing these aliquots after different intervals and titrating iodine as before.

The data obtained was applied to first order rate equation (Eqn. 1):

$$k_1 = \frac{2.303}{t}\log\frac{a}{a-x} \quad \text{……..,,,,,,} (1)$$

Where k_1 is the specific reaction rate, a, is the initial concentration of iodine at zero time and x is the amount of iodine consumed in time t.

Kinetic measurements were made by varying various parameters such as concentration of acetophenone, amino acid, acetic acid, dimethyl formamide and temperature.

RESULTS AND DISCUSSION

1. Variation of Acetophenone concentration (substrate): Kinetics of enolisation of was investigated at different time intervals (Table 1) ranging from 0-115 min and varying concentration doses of acetophenone (Table 2) from $10.0(M\times10^3) - 20.0(M\times10^3)$.

The observations clearly indicated that with the passage of increasing reaction time and increasing concentration of the substrate, the rate was found to increase mainly due to the presence of more active sites. The rate constant values obtained in absence of the amino acids were about three times less than in their presence.

The order was found to be unity, since the pseudo first order rate constant when divided by the molarity of the substrate resulted in constant units (L. mol^{-1} min^{-1}). The plot of log a/a-x vs. time (Figure 1) give straight line passing through the origin and also the slopes of the plots of log k_1 vs. log (ketone) (Figure 2) molarity was found to be approximately unity, which establishes the dependence of rate on concentration of acetophenone.

Table 1 Studies at Different Time Intervals (Temp: 50 C)
[β alanine]= 0.1M, [Iodine]=0.006M, [AcOH]=20% (v/v), [Acetophenone]=0.01M

S. No.	Time (minutes)	Volume of hypo (ml)	log a/(a-x)	$k_1 \times 10^3$ (min^{-1})
1	0	8.6	-	-
2	19	6.9	0.0957	11.59
3	37	5.5	0.1941	12.08
4	49	4.7	0.2624	12.33
5	62	4.05	0.327	12.14
6	76	3.5	0.3904	11.83
7	87	3.0	0.4574	12.10
8	96	2.6	0.5195	12.46
9	115	1.9	0.6557	13.13

Table 2 Enolisation of Acetophenone
[β alanine]= 0.1M, [Iodine]=0.006M, [AcOH]=20% (v/v)

S. No.	Acetophenone ($M \times 10^3$)	$k_1 \times 10^3$ (min^{-1})
1	10.0	3.381
2	12.0	3.920
3	14.0	4.388
4	16.0	5.049
5	20.0	5.967

Figure 1:Enolisation of Acetophenone at 60^0C

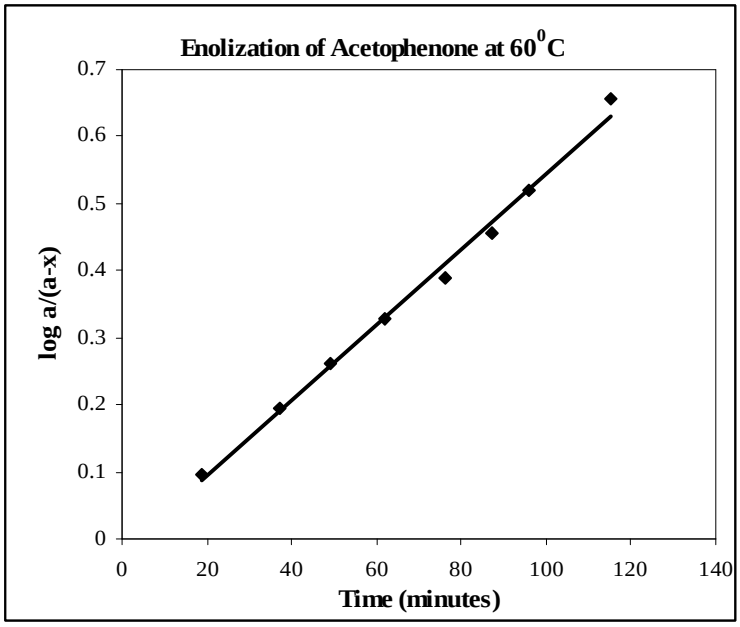
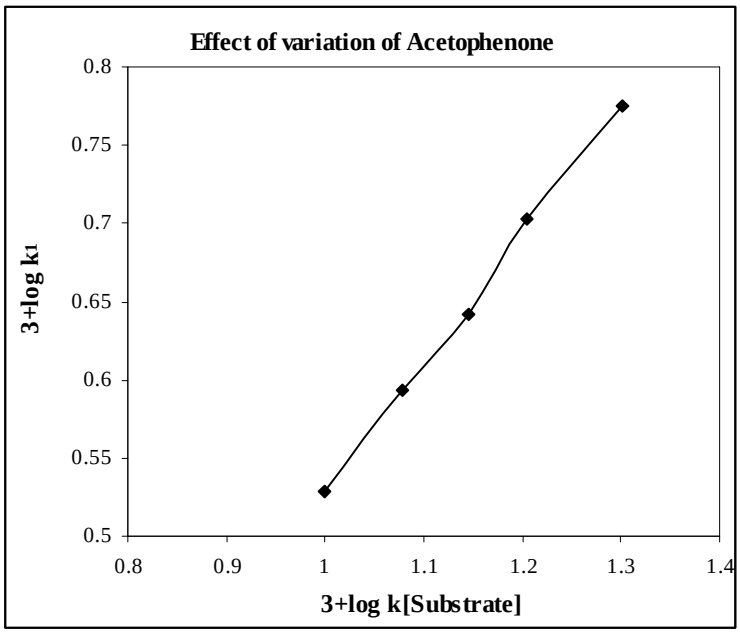


Figure 2: Effect of variation of Acetophenone



2. Effect of variation of Amino Acids (catalyst): Catalyst concentration was varied from 0.1 to 0.2 M. With the increase in the concentration of the catalysts, the activation energies significantly decreased thereby accelerating the reaction.

Table 3 Comparison of the rates of enolisation in four Amino Acids (Temp: 50 °C)
[Ketone]=0.01M, [Iodine]=0.006M, [AcOH]=20% (v/v)

S.No.	Amino Acid ($M\times10^2$)	2+ log[Acid] M	4 +log k_1			
			β alanin	DL alanin	L alanin	glycine
1	10.0	1.000	3.5211	3.3286	3.2931	3.3978
2	14.0	1.1461	3.6504	3.3726	3.3634	3.5146
3	18.0	1.2553	3.7702	3.4620	3.4213	3.5914
4	20.0	1.3010	3.8414	3.5246	3.4600	3.6162
5	22.0	1.3424	3.8652		3.4961	3.6468

Zwitter ion species of the amino acid was found to catalyse the reaction [32]. A comparative account of four different amino acids namely, glycine, β alanine, DL alanine and L alanine was also taken into consideration for through understanding of the catalytic effects. The four amino acids were expected to have different catalytic effect by virtue of the difference in the dipole moment values (glycine-13.3, β alanine-17.4, DL alanine-14.2 and L alanine-6.4). The increase or decrease in the catalytic activity was directly related to the dipole moment [33] .The data (Table 3) obtained showed the maximum catalytic activity for β alanine because of its maximum dipole moment. These values further decreased for DL alanin< L alanin in consonance with their dipole moment values. Glycine however shows a comparable dipole moment and hence rate constant values to DL alanin.

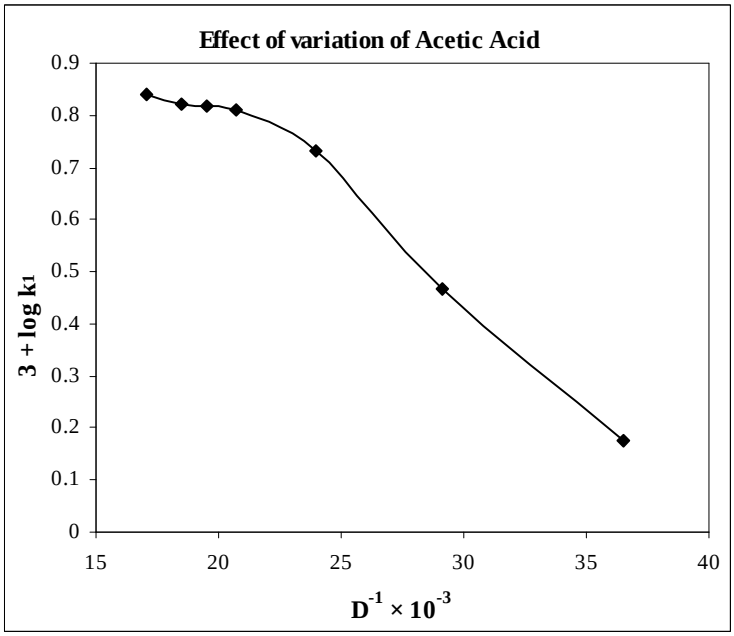
3. Effect of variation of Acetic Acid (Solvent 1): Kinetic runs were performed by varying the percentage of acetic acid (v/v) and keeping the concentration of the other reagents constant. Table 4 summarizes the results of such findings which indicate that pseudofirst order rate constant decreases with the increase in the percentage of acetic acid.

Table 4 Effect of variation of Acetic Acid (Temp: 55 ºC)
[β alanine]= 0.1M,[Iodine]=0.006M, [Acetophenone]=0.01 M

S.No.	Acetic Acid (v/v)	$k_1 \times 10^3$ (min^{-1})
1	20	6.898
2	30	6.618
3	35	6.594
4	40	6.484
5	50	5.393
6	60	2.938
7	70	1.500

The increase in value of rate constant of the enolisation with the increase in dielectric constant can be ascribed to the formation of activated complex more polar than the reactants. The plots of log k_1 vs. 1/D (Figure 3) were non linear as expected. The deviation in linearity is believed to be due to selective salvation by higher D component (water) of mixed solvent.

Figure 3:Effect of variation of Acetic Acid



Enolization of ketones proceeded faster in aqueous acetic acid than in pure acetic acid. This is in consonance with the theory that reactions involving development of charge in the transition state are facilitated by increasing the ionizing power of the solvent, and the reaction under investigation involved initially neutral molecules and polarized species.

4. Effect of variation of Dimethyl Formamide(Solvent 2): The rate of enolisation DMF/water binary mixture was found to increase by increasing the percentage composition of the solvent(Table 5). DMF being a dipolar aprotic solvent [34] and the transition state being large, cation was likely to be solvated more than the initial state. This change in solvation decreased the activation energy thereby increasing the rate. As depicted in the table the percentage composition of dimethyle formamide 50 %(v/v) in solution showed the maximum value of rate constant (0.86) than the solutions containing 10-40 %(v/v) of DMF. A regular gradation in the rate constant values with the increasing percentage composition of the solvent is noteworthy.

Table 5 Effect of variation of Dimethyle Formamide(Temp: 50 ºC)
[Ketone]= 0.01M, [Iodine] =0.006M, [β alanine]= 0.1M

S.No.	Dimethyl Formamide (v/v)	$k_1 \times 10^3$ (min^{-1})
1	10	2.993
2	20	3.336
3	30	3.735
4	40	6.186
5	50	7.266

A clear comparison between rate constants of the two solvents can be drawn in the range of 20-50 %(v/v) where the values decrease from 6.8-1.5 for acetic acid and increase from 2.9-7.2 for DMF due to the change from protic to dipolar aprotic trait.

5. Effect of Temperature: Kinetic runs were performed in the range of 45ºC to 60ºC, keeping concentration of other reagents constant. The specific rate constant k_2 is defined as in eqn.(2).

$$k_2 = \frac{k_1}{[ketone] \times 60} \text{ .....(2)}$$

The values of the rate constant obtained have been depicted in Table 6A.

Table 6(A) Effect of Temperature (K)
[Ketone]= 0.014M, [Iodine] =0.006M, [β alanine]= 0.1M, [AcOH]=20% (v/v)

S.No.	Temperature(K)	$1/T \times 0^5$	k_2 (k_1/subs.conc.) L. mol^{-1} min^{-1}	2 + log k_2	5 + log k_2/T
1	318	314.4	0.2014	1.3038	1.7986
2	323	309.5	0.3134	1.4961	1.9821
3	328	304.8	0.4707	1.6727	2.1229
4	333	300.3	0.8164	1.9119	2.3860

The inverse of temperature and log k_2 plot (not shown) resulted in straight line proving the validity of Arrhenius equation (Eqn. 3) for this reaction.

$$k_2 = A\exp^{(-Ea/RT)} \text{.....(3)}$$

In the above equation k_2 is the rate constant, A is the frequency factor, E_a is the activation energy, R is the universal gas constant and T is the temperature in Kelvin. The values obtained for the various thermodynamic parameters calculated from Arrhenius equation , like activation energy (Ea), frequency factor (A) or (Pz), Entropy (S), enthalpy (H) and free energy (F) have been shown in Table 6B. The magnitude of these parameters confirmed bimolecular nature, of the rate determining.

Table 6(B) Various Thermodynamic Parameters (Temp: 50 ºC)

ΔE (k cal mol^{-1})	Pz (l.mol^{-1} min^{-1})	$\Delta S^{\neq}$ (e.u.)	$\Delta H^{\neq}$ (K. cal mol^{-1})	$\Delta F^{\neq}$ (K. cal mol^{-1})
19.05	2.42×10^{12}	-12.126	19.06	22.98

Specific acid catalysed enolisation of acetophenone shows a prior equilibrium between acetophenone and a proton, to form a conjugate species of acetophenone. This equilibrium is fast and followed by rate determining step, that is the action of water on the conjugate species. This is then followed by the addition of iodine across the oelifinic bond and finally the elimination of hydriodic acid thereby resulting in the occurrence of the enol.

CONCLUSION

The order was found to be pseudo first order. The reaction being first order in ketone, Zwitter ion of the amino acid was found to catalyze the reaction. It was also observed that the greater the dipole moment the greater the rate.

The rate of the reaction was found to decrease by increasing the percentage of AcOH, while it was found to accelerate by increasing the Dimethyle Formamide percentage.

Acknowledgement:
One of the authors, Dr. Swati Malhotra is thankful to the fellowship granted by CSIR for persuing this research.

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