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Research Article

Kinetics of the Enolisation Reaction of m-Nitro Acetophenone Catalyzed by Amino Acids

Swati Malhotra[1], Dipika Jaspal[2]*

[1] *Department of Chemistry, SLP Science College Gwalior, Madhya Pradesh, India*

[2] *Department of Applied Science, Symbiosis Institute of Technology, Symbiosis International University, Lavale, Pune, Maharashtra, India*

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Abstract

m-Nitroacetophenone has been chosen for the study of kinetics of enolisation. Enolisation reactions have been carried out using four different amino acids viz. ß-alanin, DL-alanin, L-alanin and Glycine. The rate of the reaction has been studied by iodination. Kinetics of the reaction has been monitored under several conditions by variation of ketone concentration, dielectric constant of the medium, temperature, effect of catalysts, etc. for the enolisation process. The rate of enolisation has been found to increase with the increase in ketone concentration, percentage composition of the solvent mixture and also with the increase in the dipole moments of the amino acids. Pseudo first order rate kinetics has been found to be operational and the rate constants have been found to increase with the increase in the amino acid molarities. Linear plots obtained for log of rate constants versus reciprocal of temperature have been in good agreement with the Arrhenius equation. The values of thermodynamic parameters, like entropy ($\Delta S\neq$), enthalpy ($\Delta H\neq$), energy of activation (ΔE_a), and Gibbs free energy ($\Delta G\neq$), have been calculated which were 2.6186 e.u., 20.85 e.u., 23.46 kcal.mole^{-1} and 20.0 kcal.mole^{-1}, respectively.

Keywords: Amino Acids; Catalysis; Enolisation; Kinetics; m-Nitro acetophenone

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1. Introduction

Isomers of aldehydes and ketones are known as enols. In enols, the hydrogen is removed which attaches itself to the oxygen atom of the carbonyl group. The carbonyl compounds which are capable of forming enols are the ones which have an alpha hydrogen atom. The reversible formation of enols from enolisable ketones is known as the process of enolisation [1].

Such kind of kinetic studies have been performed on many other compounds, in some of which first order rate kinetics was operational [1-5]. In the present research the enolisation kinetics of m-Nitro acetophenone (belonging to the parent compound acetophenone), catalysed by amino acids has been studied. The enols formed during enolisation are highly reactive towards electrophiles like Iodine. Hence, the rate of enolisation has been studied by measuring the rates of iodination [6]. Enolisation reactions depend upon a number of factors like tem-

* Corresponding Author.
E-mail: sheriedipika_k@yahoo.co.in (D. Jaspal)
Tel: +91-020-39116454, Fax: +91-020-39116260

perature, concentration, nature of the catalyst etc. [7]. The main focus of the present research was to investigate the kinetics behind the enolisation process in several conditions especially in the presence of amino acids like ß-alanin, DL-alanin, L-alanin and Glycine as catalyst.

According to the available relevant data there is no substantial kinetic study taken up on m-Nitroacetophenone and hence this has been the main motivation behind the mentioned research. The present study leads to the understanding of the kinetic behavior of m-Nitroacetophenone under different conditions, which has not been studied significantly up to now.

2. Materials and Methods

m-Nitroacetophenone (A.R. grade) was procured from Bochringer-Ingelheim Germany. It was made into a stock solution (0.1 M) after dissolving it in 100% acetic acid (British Drug House). This stock solution was further used for the preparation of solutions of required concentration, after diluting with the required quantity of distilled water.

Amino acids, such as: ß-alanin, DL-alanin, L-alanin and Glycine, were procured from Renal (Budapest, Hungary) Kochloght laboratoried, ltd (Colnbrook Bucks, England), Kochloght laboratoried, Ltd (Colnbrook Bucks, England), and Chemapol (Praha, Czechoslovakia), respectively. These were made into 1M stock solutions after dissolution in bidstilled water. Amount of 0.1 M hypo solution (British Drug House) was prepared in distilled water to which 2-3 drops of chloroform was added for the stability of the solution. Standardization of hypo solution was carried out with $CuSO_4$ solution iodometerically, using starch (Reidel A.R.) as an indicator. Iodine solution (British Drug House) used for the titration was prepared by dilution from 0.1 M stock solution. NaCl required for the investigation was procured from Glaxo laboratories and was made into a 2 M stock solution for the study.

2.1. General methodology

Below mentioned general procedure was adopted in all the titrations with the variations in specific conditions mentioned under separate heads. Set of standard flasks were used for the determination, one containing ketone solution (0.1 M) and the others containing the reactant solutions (45 ml), of known concentrations prepared in distilled water. These were thermostated at 50 °C. 5 ml of the ketone solution was withdrawn from the flask containing the ketone solution and added to second flask. The time at which the ketone is introduced in the reactant mixture is noted using a stop watch. The mixture was shaken thoroughly. Amount of 5 ml of the aliquot was withdrawn immediately, quenched in ice cold water in a 100 ml flask and titrated against standard hypo solution (3×10^{-3} N) using starch indicator, in order to determine the amount of iodine liberated. This iodine indicated the amount at zero time. The study of progress of the reaction was done by such withdrawals of 5 ml aliquots from the reaction flask, done at definite intervals of 10-15 min, to determine the concentration of iodine solution at definite intervals. The amount of iodine was determined in a similar way, from zero to ninety minutes. The rate of the reaction (k_1) was determined by the appearance of the enol form of the ketone [8] according to the below given Equation (1):

$$k_1 = \frac{2.303}{t}\log\frac{a}{a-x} \qquad (1)$$

where, k_1 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.

2.2. Variation of the ketone concentration

To study the effect of variation of ketone concentration on the rate of enolisation, a range of ketone solutions from 1×10^{-2} M to 2×10^{-2} M were selected. Amount of 1 M ketone from the stock was taken and solutions of different concentration of the ketone were prepared. The concentrations of the amino acids and the solvent were kept constant.

2.3. Variation of dielectric constant

To investigate the influence of dielectric constant on the rate of enolisation, solutions of acetic acid-water and DMF-water were used and distilled before using. The concentrations of the other reactants were kept constant, and different percentage concentrations of acetic acid and DMF with water were tried. The rate constants of first order [9,10] were calculated as per Equation 1. The values of dielectric constants were taken from literature, which were 6.2 for acetic acid, 36.71 for DMF and 80.4 for water [11].

2.4. Variation of Catalyst

For the study of the effect of catalyst, amino acid concentrations ranging from 8×10^{-2} M to

5×10^{-2} M were selected and the same procedure for the study was adopted as mentioned in Section 2.1., except to the concentrations of the amino acids which were altered.

2.5. Variation of H^+ ion concentration

The effect of H^+ ion concentration on the kinetics of enolisation was investigated in the range of 0.1 to 0.5 M HCl for m-Nitroacetophenone. Stock solution of 2 M concentration was prepared and studies were carried out by varying the concentration of HCl and keeping the other reactants and temperature constant. Different hydrogen ion concentrations were expected to show different enolisation in different acid ranges.

2.6. Variation of NaCl

In order to portray the effect of natural salts on the rate of enolisation, kinetic studies for the variation in the concentration of NaCl were carried out in a range of 1 to 0.5 M NaCl, with no change in the concentrations of the other reactants.

2.7. Effect of Temperature

The applicability of Arrhenius equation was tested at four different temperatures, i.e. 318, 323, 328, and 333 K. From the iodometeric measurements, the first order rate constants were calculated [9,10] which were plotted against reciprocal of the absolute temperature. The values of the slopes and intercepts were further used for the calculation of different thermodynamic parameters such as energy of activation (E_a) [12], entropy of activation ($\Delta S\neq$), frequency factor (log Pz or $A = 10^{11}$) [13], enthalpy of activation ($\Delta H\neq$) and Gibbs free energy ($\Delta G\neq$), which were calculated as follows:

$$k_1 = A\exp^{(-Ea/RT)} \quad (2)$$

$$E_a = 2.303 \times slope \times 1.99 \times 10^{-5} \quad (3)$$

$$\log PZ = \log A = \text{int}\,erceptT^{-1} \quad (4)$$

$$PZ = \frac{KT}{h.} e^{\frac{\Delta S^{\#}}{R}} \quad (5)$$

$$A = 10^{13}.e^{\frac{\Delta S^{\#}}{R}} \quad (6)$$

$$\Delta G^{\#} = \Delta H^{\#} - T\Delta S^{\#} \quad (7)$$

Here, K is the Boltzmann constant, h is the Plank's constant, T is the absolute temperature, and R is the universal gas constant. The values of the Arrhenius parameters obtained were used to understand the nature of the reaction

3. Results and Discussion

3.1. Variation of the ketone concentration

The plots of log $a/(a-x)$ against time resulted in a straight line passing through the origin (Figure 1) indicating the first order kinetics. First order rate constants were calculated by varying the ketone concentration (Table 1), which showed an increase with the increase in the ketone concentration. Table 2 also potrays a similar direct relationship of increase in rate constant with the increase in the time interval.

As per the results reported [14], iodination of the parent compound acetophenone is an electrophilic bimolecular reaction in which the

Table 1. Rate constants corresponding to different time intervals. [m-Nitroacetophenone] = 0.016 M, [β-alanine] = 0.1 M, [Iodine] = 0.006 M, AcOH = 20 %(v/v) and Temperature = 50 °C

S. No.	[m-Nitroacetophenone] $M\times10^3$	$k_1\times10^3$ min^{-1}
1.	10.0	5.8440
2.	12.0	5.910
3.	14.0	7.233
4.	16.0	8.445
5.	18.0	9.749
6.	20.0	10.47

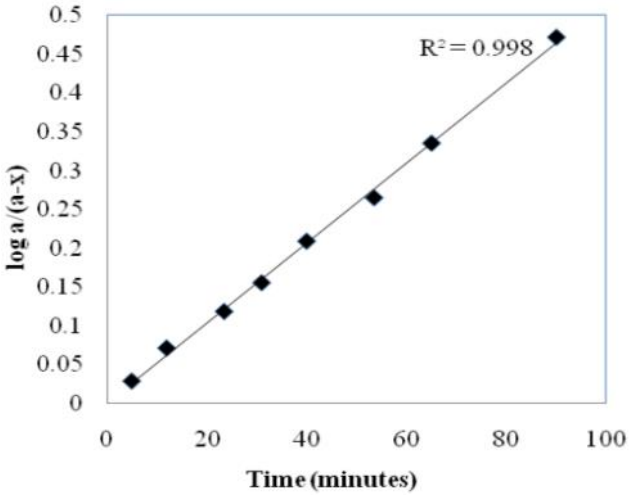


Figure 1. Plot of variation of ketone concentration vs. time

coordination between the catalyst and the ketone occurs first and then the formation of the enol takes place, the latter being a slow step determines the rate.

3.2. Variation of dielectric constant

Dimethyl Formamide (DMF) has been used as a solvent for the study of dielectric constant on the rate of enolisation. The rate was found to increase with the increase in the percentage composition of the solvent mixture (Table 3), implying that the results are in good agreement as per the theory put forward by Parker [15]. The findings support that both the solvent solute interaction and the dielectric constant are important and none can be neglected. The increase in the rate with the increase in the mole percentage of the organic solvent indicated that the factors influencing the rate are of two types, both of which work contradictory to each other and hence the overall rate would depend upon the magnitude of these factors. According to Parker and Tomilison [16] whenever a solvent like DMF is added to water, a breakdown of the water–water interaction in the molecules of water takes place.

Hence, it was found probable that the solvent (DMF) enters the structure broken portion of the solvation sheet of different ionic region. Also, DMF being a dipolar aprotic solvent and having an ion dipole type of mechanism, the transition state is large and it is likely to be solvated more than the initial state [17]. This variation in the salvation decreases the activation energy and hence increases the rate.

Table 2. Effect of variation of m-Nitroacetophenone. [β-alanine] = 0.1 M, [Iodine] = 0.006 M, AcOH = 20 %(v/v), and temperature = 50 °C

S. No.	Time Minutes	Volume of Hypo, ml	Log $a/(a-x)$	$k_1 \times 10^3$ min^{-1}
1.	0	8.0	-	-
2.	5	7.5	0.028	12.89
3.	12	6.8	0.0706	13.45
4.	23.5	6.1	0.1178	11.54
5.	31	5.6	0.1549	11.50
6.	40	4.95	0.2085	12.00
7.	53.5	4.35	0.2646	11.39
8.	65	3.7	0.3349	11.86
9.	90	2.7	0.4717	12.07

3.3. Variation of catalyst

Different catalysts (amino acids) show different values of dipole moments and are hence

Table 3. Effect of variation of dimethylformamide. [Ketone] = 0.1 M, [β-alanine] = 0.1 M, [Iodine] = 0.006 M, and temperature = 50 °C

S. No.	Dimethylformamide % v/v	$k_1 \times 10^3$ min^{-1}
1.	10	5.740
2.	20	8.051
3.	30	11.49
4.	40	13.08
5.	50	15.22
6.	60	29.69

Table 4. Comparison of the rates of enolisation of four amino acids. [Ketone] = 0.01 M, [β-alanine] = 0.1 M, [Iodine] = 0.006 M, AcOH = 20 %(v/v) and temperature = 50 °C

S. No.	[Amino acid] $M \times 10^2$	2+log acid M	4+log k min^{-1}			
			β-alanin	DL-alanin	L-alanin	Glycine
1.	8.0	0.9031	1.6542	-	-	-
2.	10.0	1.0000	1.7021	1.3874	1.3733	1.4840
3.	12.0	1.0792	1.7259	-	-	-
4.	14.0	1.1461	1.7448	1.4393	-	-
5.	15.0	1.1761	-	-	1.4402	1.5401
6.	16.0	1.2041	1.7603	-	-	-
7.	18.0	1.2553	1.8268	1.5271	-	-
8.	20.0	1.3010	1.9133	1.5560	1.4821	1.6076
9.	22.0	1.3424	-	1.5846	-	-
10.	24.0	1.3802	-	1.6030	-	-
11.	25.0	1.3979	-	-	1.6042	1.7233
12.	30.0	1.4771	-	-	1.6833	1.8267
13.	40.0	1.6021	-	-	1.7524	1.9339

expected to show different catalytic effects [18-22]. Table 4 shows the effect of variation of the amino acid concentration on the rate of enolisation. Studies were carried out in acetic acid as a solvent (20 %v/v), and the results clearly indicated that at a particular temperature pseudo first order rate constants increase with the increase in the amino acid molarities. According to literature, the amino acids in the state of equilibrium involve three kinds of species. A dipolar ionic species (Zwitter ion) exists at pH 6.0 which gets converted into a more protonated acid form with a positive charge on nitrogen [23]. With the decrease in pH however it gets converted to a more anionic species with a negative charge on oxygen. According to this investigation, the rate of enolisation of cyclic ketones increases with the increase in the amino acid concentration. The greater is the dipole moment of the amino acid the greater is the rate.

The values of the dipole movements are L-alanine = 6.4, Glycine = 13.3 D, DL-alanine = 14.2 D, and ß-alanine = 17.4 D [18-22]. Zwitter ion is the active species which has been found instrumental in accelerating the rate of enolisation. Therefore, rate is directly proportional to the Zwitter ion concentration. The results indicated that the rates of enolisation increase with the increase in the values of dipole moments.

3.4. Variation of H^+ ion concentration

The enolisation reaction is governed by the hydrogen ion concentration of the medium. The concentration of the H^+ ions remains almost constant due to its continuous regeneration and consumption. As depicted in Table 5 the rate increased from 0.1 M to 0.5 M concentration.

3.5. Effect of temperature

Enolisation kinetics has been studied at four different temperatures as mentioned before (Table 7). Plots obtained for log of rate constants and reciprocal of temperature were in good agreement with Arrhenius equation. Different thermodynamic parameters have been summarized in Table 8 which clearly depict the bimolecular nature of the reaction rate. The order of the reaction was determined by kinetic runs after altering the concentration of the ketone and keeping the other reactants constant, in presence of ß-alanin as a catalyst, at temperatures 318, 323, 328 and 333 K. The results clearly showed that the enolisation reactions were of the first order in the substrate, as shown by the plot between the ketone molarities and the rate coefficients (Figure 2).

The mechanism can be explained using the structural representations in Equations (8) and (9).

Table 5. Effect of HCl. [Ketone] = 0.01 M, [ß-alanine] = 0.1 M, [Iodine] = 0.006 M, AcOH = 5 %(v/v), and temperature = 50 °C

S. No.	[HCl] M	$k_1 \times 10^3$ min^{-1}
1.	0.1	1.279
2.	0.2	1.375
3.	0.3	1.453
4.	0.4	1.510
5.	0.5	1.550

Table 6. Effect of ionic strength. [Ketone] = 0.01 M, [ß-alanine] = 0.1 M, [Iodine] = 0.006 M, AcOH = 5 %(v/v), temperature = 50 °C and [HCl] = 0.2 M

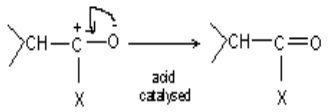
S. No.	[NaCl] M	$k_1 \times 10^3$ min^{-1}
1.	0.1	1.811
2.	0.2	1.823
3.	0.3	1.893
4.	0.4	1.812
5.	0.5	1.816

Table 7. Effect of temperature on the rate of enolisation of m-Nitroacetophenone. [ß-alanine] = 0.1 M, [Iodine] = 0.006 M, [Ketone] = 0.012 M and AcOH = 20 %(v/v)

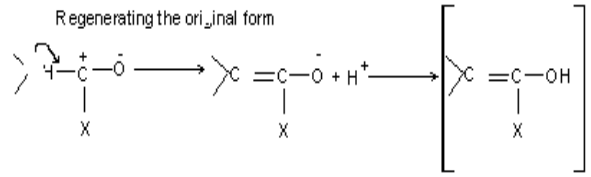
T, °K	1/T $\times 10^5$	k_2 (k_1 substrate conc.). mol^{-1} min^{-1}	2+log k_2	4+ log k_2/T
323	309.59	0.4925	1.6924	1.810
328	304.87	0.7975	1.9018	1.3816
333	300.30	1.3160	2.1192	1.5914
338	295.85	2.2960	2.6100	1.8309

Table 8. Thermodynamic parameters calculated for the enolisation of m-Nitroacetophenone. [ß-alanine] = 0.1 M, [Iodine] = 0.006 M, [Ketone] = 0.012 M and AcOH = 20 %(v/v)

ΔE_a (kcal mol^{-1})	$Pz=A$ (l.mol^{-1} min^{-1})	$\Delta S^{\neq}$ (e.u.)	$\Delta H^{\neq}$ (kcal mol^{-1})	$\Delta G^{\neq}$ (kcal mol^{-1})
23.46	3.12×10^{15}	2.6186	20.85	20.0



(8)



(9)

According to Watson, Nathan and Lourie [24] when ketone molecule collides with an acid catalyst, the energy is communicated to the groups. Therefore, in the resonance state the semipolar form becomes the main participant. An immediate transition then occurs leading to either regeneration of the original form (Equation 8) or producing the enol form (Equation 9).

4. Conclusions

Straight line plot was obtained for log $a/(a-x)$ against time which passed through the origin, thereby indicating the first order kinetics. The rate constants in the above case increased from 5.844 to 10.87 $\times 10^3$ min^{-1} when the concentration changed from 10 to 20 $\times 10^3$ M. With an increase in the mole percentage of the solvent from 10 to 16 %v/v, the rate increased approximately five folds. The results clearly showed that the enolisation reactions were of the first order in the substrate. Moreover, with the study of effect of temperature various thermodynamic parameters were calculated.

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