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ORIGINAL ARTICLE

Amino acids as catalysts for the enolisation study of m-Methylacetophenone

Swati Malhotra [a], **Dipika Jaspal** [b,*], **Arti Malviya** [c]

[a] *Department of Chemistry, SLP Science College Gwalior, Madhya Pradesh, India*
[b] *Department of Applied Science, Symbiosis Institute of Technology (SIT), Symbiosis International University (SIU), Lavale, Pune, Maharashtra, India*
[c] *Lakshmi Narain College of Technology, Bhopal, Madhya Pradesh, India*

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Abstract Amino acids have been used as catalysts for the study of kinetic of enolisation of m-Methylacetophenone, in which iodination has been the chosen method. Several parameters like effect of ketone concentration, effect of dielectric constant, effect of catalysts etc. have been investigated for their effect on enolisation kinetics. The study is focused on β-alanine, DL-alanine, L-alanine and Glycine for their effects on the rate. The order of the rate constants obtained has been found to be in the order of increasing dipole moments of the amino acids i.e. L-alanine < Glycine < DL-alanine < β-alanine. With an increase in the temperature from 323 K to 338 K, an increase in the rate was from 1.3 to 2.12 mol^{-1} min^{-1}. The ongoing reaction was found to be bimolecular in nature. The values of different thermodynamic parameters like Entropy ($\Delta S^{\neq}$), Enthalpy ($\Delta H^{\neq}$), Energy of activation (ΔEa) and Gibbs free energy ($\Delta F^{\neq}$) were found to be 6.20 e.u., 24.74 cal mol^{-1}, 25.20 k cal mol^{-1} and 24.54 cal mol^{-1} respectively.

1. Introduction

Enolisation of ketones has been an important subject of study for researchers. Several compounds have been studied for their enolisation kinetics like fructosamines (Smith and Thornalley, 1992), p-ethoxyacetophenone (Khirwar, 2010), 2- and 3-Acetylthiophenes (Maria et al., 1991), cycloheptanone (Musharan et al., 1980). As per literature, the kinetic study of enolisation on m-Methylacetophenone, derived from the parent compound acetophenone has been carried out in the presence of substances like Tl (III) Perchlorate in Perchloric Acid (Sultan et al., 2010), but still the studies on enolisation of m-Methylacetophenone in the presence of amino acids as catalysts remains a subject to be explored. Hence, this has lead to the development of interest in experimenting m-Methylacetophenone for its enolisation kinetics in the presence of amino acids. It is expected that the present research would throw light on the kinetics behind enolisation reactions and be helpful in

* Corresponding author. Tel.: +91 020 39116454; fax: +91 020 39116260.
E-mail address: sheriedipika_k@yahoo.co.in (D. Jaspal).
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understanding how one of the derivatives of acetophenone responds under different sets of environments.

m-Methylacetophenone is a colorless liquid used as a reagent in organic synthesis. Amino acids too on the other hand have been tested for their catalytic activity on a number of substances (Malhotra and Jaspal, 2014; Rodina and Godson, 2006; Zhong et al., 2012; Vassilev et al., 2013). However no substantial work has been carried out in order to study the catalytic potential of these biomolecules in the enolisation of m-Methylacetophenone which remains the main motive of this research work. Four different amino acids viz. like β-alanine, DL-alanine, L-alanine and Glycine have been chosen for the catalytic investigations.

The present research therefore mainly concentrates on the study of enolisation kinetics of m-Methylacetophenone under the influence of several factors especially in the presence of amino acids as catalysts. There are several factors governing the rate of enolisation i.e. reaction temperature, concentration of ketone, nature of the catalyst etc. (Singh et al., 1982) which have been studied for their effect on the kinetics of enolisation reaction.

2. Materials and methods

m-Methylacetophenone IUPAC name 1-(3-methylphenyl) ethan-1-one has the molecular formula $C_9H_{10}O$ and molecular mass 134.1751 of, A.R. grade was procured from Boehringer-Ingelheim Germany.

Stock solution of the ketone was made by dissolving it in 100% acetic acid (British Drug House). The solutions for experimentation were obtained after diluting this stock solution. Four different Amino acids used in the research viz. β-alanine, DL-alanine, L-alanine and Glycine were procured from Renal (Budapest, Hungary) Kochlight laboratories, ltd (Colnbrook Bucks, England), Kochlight laboratories, ltd (Colnbrook Bucks, England) and Chemapol (Praha, Czechoslovakia) respectively. 1 M stock solutions of these amino acids were made in bidistilled water. Hypo solution (0.1 M) required for the iodometric titration was made after addition of 2–3 drops of chloroform for stability of the solution. $CuSO_4$ solution was used for the standardization of hypo solution iodometrically, using starch as an indicator (Reidel A.R.). Iodine solution (British Drug House) and NaCl (Glaxo Laboratories) required for the research were prepared by dilution from stock solutions.

2.1. General methodology

Ketone solution of 0.1 M concentration was prepared and was taken in standard flask. Simultaneously in other flasks reactant solutions (45 mL) were taken, which were prepared in distilled water. All the mentioned flasks were thermostated at a temperature of about 50 °C. 5 mL of the ketone solution was withdrawn from the flask containing ketone solution and added to the flask containing reactant solution for the reaction to take place. The time of introduction of the ketone solution to the reactant mixture was noted using a stop watch. In order to determine the amount of iodine liberated iodometric titrations were carried out. 5 mL of the solution was withdrawn from the reactant flask, quenched in ice cold water in a 100 mL flask and titrated with hypo solution (3×10^{-3} N) using starch as an indicator. The amount of iodine liberated indicated the reaction taking place at zero time. Similar withdrawals from the reaction flasks were done at definite intervals of 10–15 min and the amount of iodine liberated was estimated each time. Rate constant (k_1) was calculated for the ongoing reaction which shown by the below given rate equation (Sachs, 1971):

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

In the above equation, k_1 is the specific reaction rate (sec^{-1}), a, is the initial concentration of iodine (M) at zero time and x is the amount of iodine consumed in time t (M).

2.2. Variation of ketone concentration

A range of ketone concentrations from 1.0×10^{-2} M to 2.0×10^{-2} M were prepared from 1 M stock solution to determine the effect of variation of the ketone concentration on the rate of enolisation. Enolisation reactions were carried out in a similar way (as mentioned in Section 2.1) by varying the ketone concentration and keeping the concentration of the other reactants constant.

2.3. Variation of dielectric constant

Solution mixtures of DMF-water were used in order to study the effect of dielectric constant on the enolisation kinetics. These solution mixtures were distilled before use. Different percentage compositions of DMF were experimented keeping the concentrations of the other reactants constant. Dipole moment values as per literature were 36.71 for DMF and 80.4 for water (Singh, 1981). The rate constants of first order were calculated according to Eq. (1).

2.4. Variation of catalyst

The study of the effect of catalyst was carried out in the range of 8.0×10^{-2} M to 5.0×10^{-2} M concentration of the amino acids. The general methodology of the experiments remained the same as discussed earlier and the concentration of the catalysts i.e. the amino acids was altered.

2.5. Variation of H^+ ion concentration

Solutions concentrations varying from 0.1 M to 0.5 M HCl were prepared from a 2 M stock solution. Experiments were carried out as described in Section 2.1 except for the concentration of the acid was altered. Enolisation rates for different concentrations of the acid were expected to be different.

2.6. Variation of NaCl

Salt effect was studied by carrying out the reaction in different concentrations of NaCl ranging from 1.0 M to 0.5 M, keeping the concentration of the other reactants constant.

2.7. Effect of temperature

The effect of temperature on the rate of enolisation was studied at four different temperatures, 318, 323, 328 and 333 K.

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First order rate constant was calculated as per Eq. (1) and plotted as a reciprocal of absolute temperature. Different thermodynamic parameters were calculated using the slopes and intercepts of this graph in order to understand the nature of the reaction. Different thermodynamic parameters included in the study were energy of activation (*Ea*) (Laidler, 1965), entropy of activation ($\Delta S^{\neq}$), frequency factor (log *PZ* or *A* = 1011) (Thakur et al., 2012), enthalpy of activation ($\Delta H^{\neq}$) and Gibbs free energy ($\Delta F^{\neq}$). Eqs. (2)–(7) give the mathematical expressions used for the calculation of the different parameters.

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

$$Ea = 2.303 \times slope \times 1.99 \times 10^{-5} \tag{3}$$

$$\log PZ = \log A = \text{intercept } T^{-1} \tag{4}$$

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

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

$$\Delta F^{\#} = \Delta H^{\#} - T\Delta S^{\#} \tag{7}$$

In the above equations *K* is the Boltzmann constant, h is the Plank's constant, *T* is the absolute temperature and *R* is the Universal gas constant.

3. Results and discussions

3.1. Variation of ketone concentration

As per the data obtained graphs for log $a/(a-x)$ against time were plotted which showed a straight line passing through the origin with an R^2 value of 0.99, indicating the first order kinetics. Further the value of rate constants were calculated which were found to be in good agreement with the first order criteria. Different values or rate constants calculated keeping the ketone concentration constant at different time intervals have been shown in Table 1. Table 2 shows an increase in the rate constant with the increase in the ketone concentration indicating a direct relation between rate and concentration of the ketone.

3.2. Variation of dielectric constant

The values of rate constants in Table 3 show that the rate increased substantially with the increase in the percentage composition of DMF. This implies that besides the solvent solute interaction, dielectric constant also played a vital role (Thakur et al., 2012). The readings obtained were in accordance to the theory put forward by Parker. As per the research carried out by Parker and Tomilison (Parker, 1962), on addition of a solvent like DMF there occurs a disruption in the interaction between the water molecules.

Therefore it can be derived that probably DMF enters the structure broken portion of the solvation sheet of water molecules. The structure of DMF which is dipolar and aprotic shows an ion dipole type of mechanism. Hence the transition state is large and it is expected to be solvated more in comparison to the primary state (Parker and Tomlinson, 1971; Raveendran and Neelakumari, 2012). The increase in the rate was attributed to the change in the salvations and a decrease in the activation energy.

Table 1 Rate constants after different time intervals [m-Methylacetophenone] = 0.01 M, [β-alanine] = 0.1 M, [Iodine] = 0.006 M, AcOH = 20% (v/v), temperature = 60 °C.

S. No.	Time (minutes)	Volume of hypo (mL)	Log $a/(a-x)$	$k_1 \times 10^3$ min^{-1}
1.	0	10.5	–	–
2.	10.5	9.6	0.0389	8.332
3.	19	8.95	0.0694	8.412
4.	32	8.0	0.1181	8.499
5.	40	7.45	0.149	8.578
6.	59	6.45	0.2116	8.629
7.	89	5.1	0.3136	8.634
8.	139	3.2	0.5161	8.650
9.	165.5	2.5	0.62233	8.673

Table 2 Effect of variation of m-Methylacetophenone [β-alanine] = 0.1 M, [Iodine] = 0.006 M, AcOH = 20% (v/v), temperature = 60 °C.

S. No.	[m-Methylacetophenone] M × 10^3	$k_1 \times 10^3$ min^{-1}
1.	10.0	2.45
2.	12.0	2.935
3.	14.0	3.266
4.	16.0	3.520
5.	18.0	4.314
6.	20.0	4.794

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

S. No.	Dimethylformamide% (v/v)	$k_1 \times 10^3$ min^{-1}
1.	20	3.143
2.	30	5.388
3.	40	8.518
4.	50	11.64
5.	60	20.35

3.3. Variation of catalyst

Rates were found to be directly related to the values of Dipole moments of the amino acids (Dragcbevic and Biscan, 2003; Destro et al., 1989). 20%v/v Acetic acid was used as a solvent and the results shown in Table 4 depict the interrelationship between the rates and the increase in the amino acid molarities. With the increase in the amino acid molarities at a particular temperature pseudo first order rate constants increased. Also an increase in the rate was observed with the increase in the dipole moments of the amino acids.

The values of the rate constants obtained were well in agreement with the increasing order of the dipole moments L-alanine = 6.4 < Glycine = 13.3 D < DL-alanine = 14.2 D < β-alanine = 17.4 D. Amino acids basically form a dipolar

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), temperature = 50 °C.

S. No.	[Amino Acid] M × 10^2	2 + log acid (M)	4 + log k min^{-1}			
			β-alanine	DL-alanine	L-alanine	Glycine
1.	10.0		1.5502	1.3243	1.3516	1.4370
2.	12.0	1.0000	1.6010	–	–	–
3.	14.0	1.0792	1.6405	1.3840	–	–
4.	15.0	1.1461	–	–	1.4019	1.5781
5.	16.0	1.1781	1.6749			
	–	–	–			
6.	18.0	1.2041	1.7300	1.4505	–	–
7.	20.0	1.2553	1.7709	1.4940	1.4738	1.7120
8.	24.0	1.3010	–	1.5635	–	–
9.	25.0	1.3802	–	–	1.5023	–
10.	28.0	1.3979	–	1.5988	–	–
11.	30.0	1.4472	1.8651	1.6326	1.5885	1.8167
12.	40.0	1.4771	–	–	1.6834	1.9492
13.	50.0	1.6990	–	–	–	2.0102

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

S. No.	[HCl] M	$k_1 \times 10^3$ min^{-1}
1.	0.0	1.447
2.	0.1	1.475
3.	0.2	1.515
4.	0.3	1.580
5.	0.4	1.624

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

S. No.	[NaCl] (M)	$k_1 \times 10^3$ min^{-1}
1.	0.0	2.114
2.	0.1	2.130
3.	0.2	2.150
4.	0.3	2.309
5.	0.4	2.343

ionic species (Zwitter ion) at pH 6.0 which transforms into a more protonated acid form having a positive charge on nitrogen. This then converts into an anionic species with an oxygen atom carrying a negative charge, with a decrease in the pH. It was this Zwitter ion species which was found to accelerate the rate of enolisation. Therefore there occurs a direct relationship between the rate of enolisation and the Zwitter ion concentration.

3.4. Variation of H^+ ion concentration

The rate constants were found to be dependent on the concentration of H^+ ions of the medium when investigations were carried out from 0.1 M to 0.5 M concentration (Table 5). This showed a favorable effect of the presence of protons on the rate of enolisation.

3.5. Variation of NaCl

The concentration of the salt (NaCl) was studied in the range of 0.1 M–0.4 M, keeping the concentration of the other reactants constant (Table 6). As in the other discussed cases the rate did not show a significant change with the increase in the salt concentration proving the enolisation of m-Methylacetophenone being independent of the effect of salt concentration alteration.

3.6. Effect of temperature

Kinetics of any reaction depends upon temperature and similar was observed in this case. Four different temperature ranges were considered for the study of the effect of temperature (318, 323, 328 and 333 K) using β-alanine as a catalyst. Graphs were plot for log of rate constants versus reciprocal of temperature and were found to be in good agreement with Arrhenius

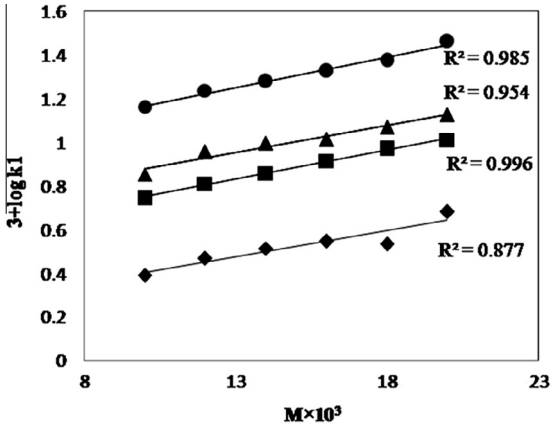

Figure 1 Plot between the ketone molarities and the rate coefficient at ♦318, ■323, ▲328 and ●333 K.

Table 7 Effect of temperature on the rate of enolisation of m-Methylacetophenone [β-alanine] = 0.1 M, [Iodine] = 0.006 M, [Ketone] = 0.016 M, 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	5 + log k_2/T
323	309.59	0.2200	1.3424	1.8334
328	304.87	0.5131	1.7076	2.1914
333	300.30	0.7343	1.8633	2.3408
338	295.85	1.3862	2.1139	2.5848

equation. With the help of these studies different thermodynamic parameters were calculated and the values were found to be 25.20 kcal mol^{-1}, 2.39×10^{16} l mol^{-1} min^{-1}, 6.20 e.u, 24.74 K cal mol^{-1} and 24.54 K cal mol^{-1} for ΔEa, $Pz = A$, $\Delta S^{\neq}$, $\Delta H^{\neq}$ and $\Delta F^{\neq}$ respectively.

The results clearly showed the bimolecular nature of the ongoing enolisation process. The R^2 values for the plot between ketone molarities and the rate coefficient (Fig. 1) were found to be 0.87.0.96, 0.95 and 0.98, at temperatures 318, 323, 328 and 333 K respectively, indicating that the enolisation process proceeded well according to the first order kinetics. Also the rate was found to accelerate with the rise in temperature (Table 7).

Watson, Nathan and Lourie (Watson et al., 1935) explained the mechanism in two stages. In the first stage the ketone molecule collides with an acid catalyst a semipolar form becomes the main participant and energy is communicated to the groups in the resonance state. The transition from the keto to the enol form takes place in the next stage immediately in the next stage.

4. Conclusions

Amino acids have been found to exhibit a predominant effect on the rate of enolisation. Salt effect also was found to be directly related to the rate of the reaction. Enolisation kinetics was directly found to be related to the values of dipole moments of the amino acids. Different thermodynamic parameters were calculated in order to understand the nature of the process. The reaction was found to be endothermic with a $\Delta H^{\neq}$ value 24.74 K cal mol^{-1}.

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