Effect of Aqueous DMSO Solvent on the Hydrolysis Rate and Mechanism of a Biologically Active Ester Methylpicolinate

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ABSTRACT:

The kinetic study of hydrolysis of Methylpicolinate in an aqueous DMSO solvent mixture was conducted conductometrically to unravel the influence of solvent composition on reaction dynamics. The reaction was examined at four different temperatures—20^0C, 25^0C, 30^0C, and 35^0C while systematically varying the solvent proportion from 10% to 60%. Interestingly, the reaction rate consistently declined as the solvent composition increased across all temperature ranges.

To gain deeper insight into the solvent effect on reaction kinetics and mechanism, key activation parameters were evaluated. Iso-composition activation energy, Iso-dielectric activation energy and various thermodynamic parameters were analyzed to provide a broader perspective on the reaction mechanism. Transition state theory drives thermodynamic approach of reaction rate and rate constant is expressed in terms of thermodynamic parameters. Kinetic study was also done in terms of water concentration.

KEYWORDS: Transition state theory, rate constant, Methylpicolinate, DMSO, Iso-composition activation energy, Iso-dielectric activation energy and solvation number.

1. INTRODUCTION:

To correlate the rate change with properties of the solvent medium a lot of works[1-7] have been carried out. It was predicted that the reactivity is influenced by solvolysis of transition state through solvent-solute interaction.

So, a study was done to investigate the effect of DMSO on alkali catalyzed hydrolysis of Methylpicolinate with a view as to how these predictions are applicable in this particular reaction and a comparative study at different composition of solvent DMSO at fixed temperature gives idea about the effectiveness of ester which is pharmaceutically important. The iso-composition activation energy, iso-dielectric activation energy and various thermodynamic parameters are also evaluated to understand the mechanism of reaction.

2. EXPERIMENTAL:

High purity grade, DMSO and Methylpicolinate were used. N/5 strength of NaOH and aqueous DMSO solvent varying in composition (10% to 60%) was made using double distilled water. A known volume is mixed and taken in conductivity cell and conductance was recorded at regular interval of time using conductivity meter. The process was done at different temperature (20^0C, 25^0C, 30^0C and 35^0C). From the results, specific rate constant in aqueous DMSO were determined as shown in **Table-1**. The reaction was found to obey second order Kinetics. The variation of logk with mole% of DMSO is shown in **Fig.-1**, using the value given in **Table-2**. Iso-composition activation energy (Ec) and Iso-dielectric activation energy (E_D) were calculated using slope of Arrhenius plot of logk vs 1/T, tabulated in **Table-4** & **Table-5** respectively. The graph was plotted in **Fig.-2**, using the value mentioned in **Table-3**. The variation of logk with log [H_2O] is mentioned in **Table-6.** Thermodynamic activation parameters were calculated using Wynne Jones and Eyring equation[8] shown in **Table-8**.

3. RESULT AND DISCUSSION:

(a) Effect of solvent on specific rate constant:

The value of specific rate constant (k) decreases with increasing proportion of organic co-solvent DMSO in the reactions mixture. For showing the solvent effect, on specific rate constant of the reaction, the logk values have been plotted against mole% of added organic co-solvent (DMSO) of reaction media as shown in Fig.-1. The perspectives of Hughes and Ingold[9], along with the predictions of Laidler and Landskroener[10], provide valuable insights into the observed rate behavior. According to their studies, a decline in the dielectric constant of the reaction medium leads to a decrease in the reaction rate.

In the present case, as the proportion of DMSO increases or the water content decreases, the dielectric constant of the medium is reduced accordingly. This decline in rate can be primarily attributed to:

1. A reduction in the polarity of the reaction medium, transitioning from a highly polar aqueous environment to a less polar water-DMSO mixture.
2. A decrease in the bulk dielectric constant of the medium, which further influences reaction kinetics.

Both these factors play a crucial role in determining reaction rates and align well with the theoretical framework proposed by the aforementioned researchers. The decrease in reaction rate with a lowering dielectric constant is, therefore, an expected outcome. Similar observations have been previously reported by Singh A.K.[11], reinforcing the consistency of these findings.

Table-1

Value of specific rate constant (k) of base catalyzed hydrolysis of Methylpicolinate in aquo-DMSO media.

Temp. in ^{0}C	**% of DMSO**					
	10%	**20%**	**30%**	**40%**	**50%**	**60%**
20^{0}C	18.62	17.78	17.37	16.59	15.84	15.48
25^{0}C	25.11	23.44	21.87	20.41	19.05	18.19
30^{0}C	31.62	29.51	26.91	24.54	22.38	20.89
35^{0}C	41.68	38.01	33.88	30.90	26.91	24.54

Table-2

Variation of logk values of the reaction with mole % of DMSO in aquo-DMSO media at different temperature.

% of DMSO (v/V)	Mole % of DMSO	logk			
		20^{0}C	25^{0}C	30^{0}C	35^{0}C
10%	2.597	1.27	1.40	1.50	1.62
20%	5.633	1.25	1.37	1.47	1.58
30%	9.204	1.24	1.34	1.43	1.53
40%	13.520	1.22	1.31	1.39	1.49
50%	18.736	1.20	1.28	1.35	1.43
60%	25.32	1.19	1.26	1.32	1.39

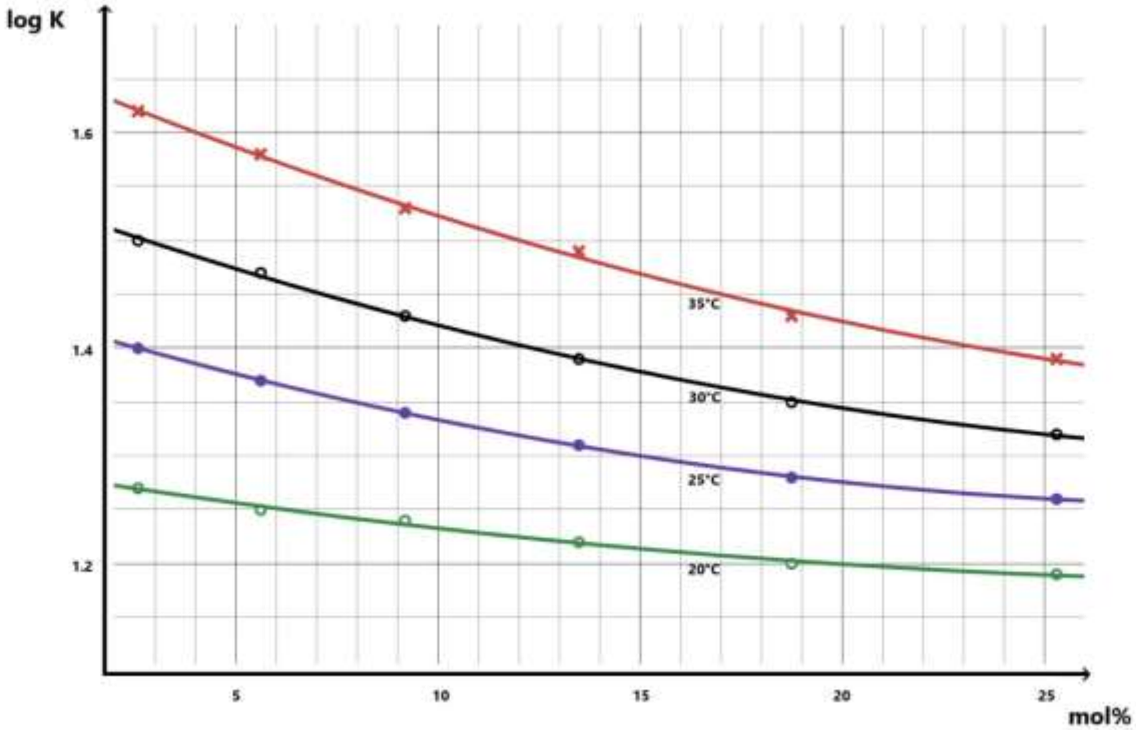

Fig. -1 variation of logk values with mole % of DMSO in water-DMSO media.

(b) Iso-composition activation energy (Ec) of the reaction:

It was observed from the **Table-4** that the value of iso-composition activation energy (Ec) decreases with increase in the concentration of organic co-solvent DMSO in the reaction mixture. This is because of solvation changes at transition state level. This reduction in Ec values can be attributed to the solvation effects and can be explained by the following scenarios:-

1. The transition state becomes solvated while the initial state is desolvated.
2. The transition state is solvated more strongly than the initial state.
3. The initial state is desolvated more strongly than the transition state.

Among these, the first one is the most likely explanation. The reduced entropy of activation (ΔS*) and enthalpy of activation (ΔH*), as recorded in Table-8 indicates that solvation stabilizes the transition state lowering the energy required for the reaction to proceed.

Furthermore, similar conclusions have been drawn by Singh A.K.[12], reinforcing the validity of this interpretation. Recently reported research by Lal and Singh et al.[13] and N. K[14] also support the conclusion.

Table-3

Variation of logk values of the reaction with $10^3/T$ in aquo-DMSO media.

Temp. in ^{0}C	**10^3/T**	**log k**					
		10%	**20%**	**30%**	**40%**	**50%**	**60%**
20^{0}C	3.41	1.27	1.25	1.24	1.22	1.20	1.19
25^{0}C	3.35	1.40	1.37	1.34	1.31	1.28	1.26
30^{0}C	3.30	1.50	1.47	1.43	1.39	1.35	1.32
35^{0}C	3.24	1.62	1.58	1.53	1.49	1.43	1.39

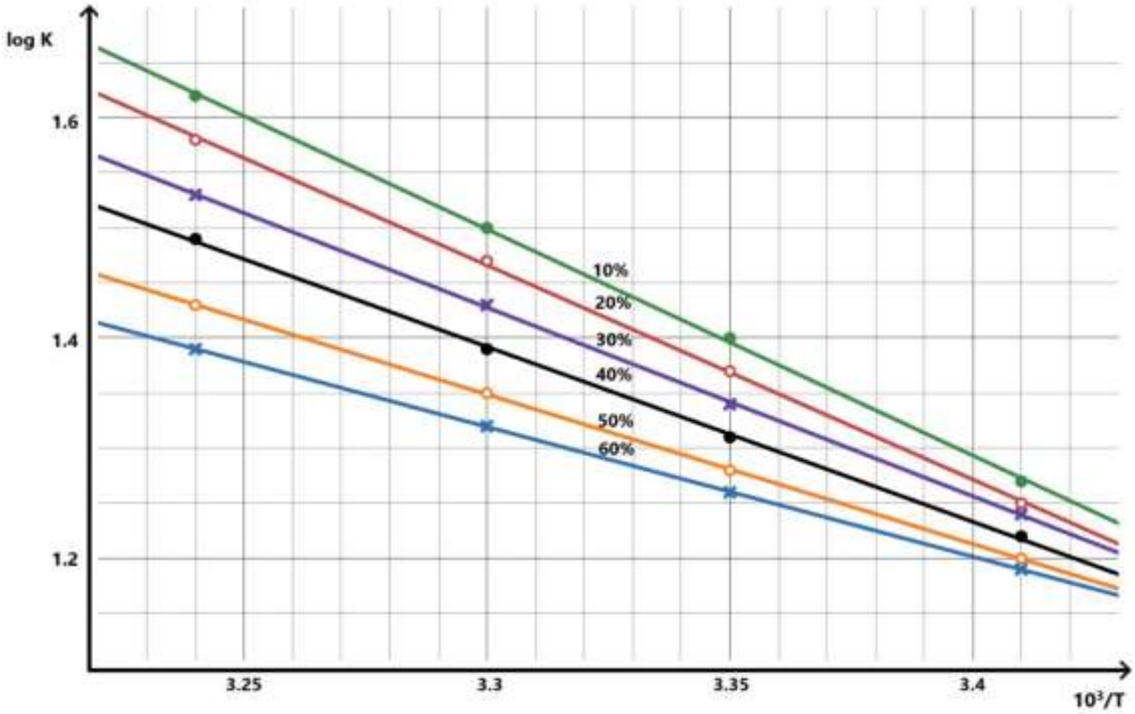

Fig.-2: Plot of logk vs. $10^3/T$ in aquo-DMSO media

Table -4

Values of Iso-composition activation energy of the base catalyst reaction of Methylpicolinate with increasing percentage of solvent DMSO.

% of DMSO (v/V)	10%	20%	30%	40%	50%	60%
Ec values in KJ/mol	39.25	37.24	32.79	30.42	25.96	22.56

(c) Iso-dielectric activation energy (E_D) of the reaction:

Iso-dielectric activation energy was calculated from the slope of $\log k_D$ (obtained from interpolation of plots of logk value against D value of reaction media) against 1/T at different dielectric constant values as mentioned in **Table-5**.

Table-5

Evaluated values of Iso-dielectric activation energy (E_D) of the reaction at different dielectric constant D of the aquo-DMSO media.

Value of D	D=72	D=74	D=76	D=78	D=80	D=82
E_D values in KJ/mol	39.94	48.53	55.67	62.19	69.02	75.85

From Table-5 it was found that the value of E_D increases with increasing di-electric constant value of the reaction media. This trend of variation in E_D is supported by Wolford[15].

(d) Solvent effect on solvation number and mechanistic path of the reaction:

The slope of the plot logk against log [H_2O] gives the number of water molecule i.e. solvation number (n) associated with the activated complex using Robertson equation[16];

$$\log k = \log k' + n \log [H_2O]$$

It tells about the criterion for studying about the mechanism of the reaction. The value of logk and log [H_2O] are tabulated in Table-6 and plots are shown in Fig.-3. The value of slope of the plot i.e. solvation number has been tabulated in Table-7. Robertson et al.[17] established that the solvation number (n) of water molecules surrounding the activated complex is significantly higher in unimolecular reactions and lower in bimolecular pathways. Data from **Table-7** clearly indicate that the solvation no. (n) decreases with increasing concentration of DMSO and increases with increasing temperature of the reaction media. According to the findings of Robertson et al.[17], the mechanistic path followed by the reaction changes from bimolecular to unimolecular with rise in temperature because of increase in the no. of n and unimolecular to bimolecular with gradual addition of solvent DMSO in the reaction media.

Additionally, it is concluded that the addition of DMSO shifts the equilibrium of water molecules from their dense form to a bulkier, less compact form.

$$(H_2O)_d \rightleftharpoons (H_2O)_b$$

This interpretation is further supported by the findings of Arjuman Bano et al.[18], reinforcing the concept of solvent-induced structural transformation of water under different reaction conditions.

Table-6

Variation of the values of logk with log [H_2O] value of aquo-DMSO media at different temperatures.

% of DMSO (v/V)	% of H_2O	log [H_2O]	logk			
			20^0C	25^0C	30^0C	35^0C
10%	90%	1.60	1.27	1.40	1.50	1.62
20%	80%	1.55	1.25	1.37	1.47	1.58
30%	70%	1.49	1.24	1.34	1.43	1.53
40%	60%	1.42	1.22	1.31	1.39	1.49
50%	50%	1.346	1.20	1.28	1.35	1.43
60%	40%	1.24	1.19	1.26	1.32	1.38

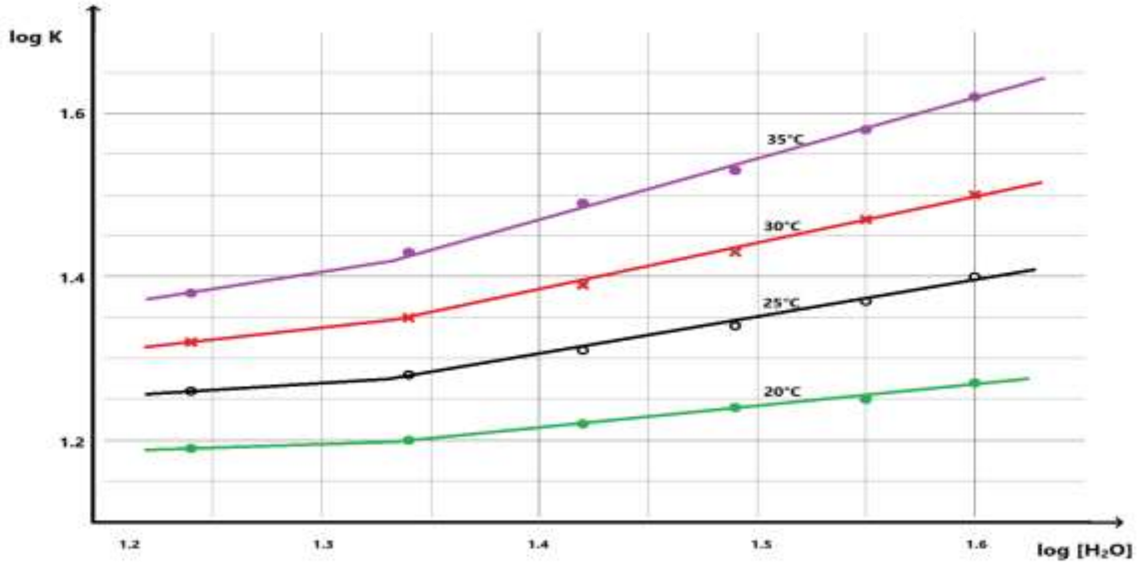

Fig.-3: variation of logK values against log[H2O] values in aquo-DMSO media.

Table-7

Values of the slopes of the plots of logk verses log [H_2O] at different temperatures.

Temp. in ^0C	Slope- I when log [H_2O] is below 1.344 (49.90%)	Slope-II when log [H_2O] is above 1.344
20^0C	0.0710	0.260
25^0C	0.115	0.457
30^0C	0.153	0.582
35^0C	0.350	0.735

(e) Solvent effect on thermodynamic activation parameters:

It was observed from Table-8 that the value of the ΔH^* and ΔS^* decreases while ΔG^* increases with increase in mole% of the organic co-solvent DMSO in the reaction media.

The thermodynamic relation **(**$\Delta G^* = \Delta H^* - T\Delta S^*$), inferred that the simultaneous increase in ΔG^* with decline in ΔH^* and ΔS^* is only possible if the decline in ΔS^* is more pronounced than that of ΔH^*. It indicates that in this case of hydrolysis the driving force of the reaction is enthalpy change. However, entropy plays a crucial role in controlling the reaction. This observation is also supported by Singh et al.[19].

Table-8

Evaluated values of thermodynamic activation parameter (ΔH^* ΔG^* and ΔS^*) of the base catalyzed hydrolysis of Methylpicolinate in aquo – DMSO media at different mole percentage of DMSO and different temperatures.

ΔH^* and ΔG^* in KJ/mole, ΔS^* in J/K/mole

% of DMSO (v/V)	**Mole % of DMSO**	**ΔH^* in KJ/mole**	**20^0C**		**25^0C**		**30^0C**		**35^0C**	
			ΔG^*	**ΔS^***	**ΔG^***	**ΔS^***	**ΔG^***	**ΔS^***	**ΔG^***	**ΔS^***
10%	**2.59**	**38.29**	64.59	-89.79	65.00	-89.65	65.55	-89.99	65.96	-89.87
20%	**5.63**	**34.65**	64.70	-102.59	65.17	-102.43	65.72	-102.57	66.20	-102.46
30%	**9.20**	**31.78**	64.77	-112.60	65.34	-112.64	66.01	-112.99	66.50	-112.73
40%	**13.52**	**29.86**	64.88	-119.53	65.51	-119.65	66.19	-119.91	66.30	-119.73
50%	**18.73**	**26.23**	64.99	-132.30	65.68	-132.41	66.42	-132.65	67.09	-132.67
60%	**25.32**	**20.18**	65.05	-153.13	65.78	-153.04	66.59	-153.20	67.32	-153.07

4. CONCLUSION:

From the evaluation of the reaction framework, the following conclusions have been established:

1. The reaction rate decreases as the dielectric constant of the medium declines.
2. The reduction in iso-composition activation energy suggests that the transition state is solvated, while the initial state remains desolvated.
3. The iso-dielectric activation energy increases with increase in dielectric constant of the reaction media.
4. A rise in the number of water molecules associated with the activated complex indicates a shift in the reaction mechanism from a bimolecular to a unimolecular pathway with increase in temperature.
5. Alkali catalyzed hydrolysis of Methylpicolinate in water DMSO media is enthalpy driven and entropy controlled.

5. REFERENCES:

1. D. K. Verma, Brahmeshevar, Prahlad Kumar and R.K. Lal : ISACM, 575-577, 2020.

2. Singh AK. : Activation parameters and solvent effect on solvolysis of ethyl benzoate in aquo-organic solvent system. Asian journal of research in chemistry, 2019, 12(2).

3. Singh AK. A Kinetics study of Solvent Effect and biological behavior of Hexanoate ester in water propanol solvent system. Journal of Applied Chemical Science, https://doi.org/10.22341/jacson.00xxx,Dec, 2018.

4. Singh AK. Kinetics and dipolar protic solvent effect on activation parameter of base catalyzed hydrolysis of propyl Hexanoate in aquous solvent system. Journal of Applied Chemical Science, https://doi.org/ 10.22341/ jacson.00xxx, 2018.

5. Singh A K., Arjuman Bano: Kinetics and Solvent effect on Aquo-dipolar protic organic-solvent system of Hexanoate ester." Asian journal of Research in Chemistry, 12(6) Nov 2019, pp 341-344.

6. Singh AK. The influence of solvent on solvolysis of ethyl cinnamate in water-acetone mixed solvent system. ISBN: 978-0-9957075-3-5, International Journal of Engineering and applied Computer, Vol-02, Issue 02, Feb, 2017, pp. 79-82.

7. Magda Fathalla F. Kinetics of Reaction of 2-Chloroquinoxaline with Hydroxide Ion in CAN-H2 O and DMSO-H2O Binary Solvent Mixture", J. Solution Chem. 2011; 40:1258-70.

8. Wynne-Jones WF, Eyring H. The absolute rate of reaction in condensed phases. J. Chem Phy. 1935; 3:492-502.

9. Hughes ED, Ingold CK. Mechanism of substitution at saturated carbon atom part IV, A discussion of constitution and solvent effect on mechanism, kinetics, velocity, and orientation of substitution. j chem. Soc, 1935, 244-255.

10. Laidler KJ, Landskroener PA. Influnce of solvent on reaction rate. Transaction of Farady society. 1956; 52:200.

11. Singh AK. solvent effect on enthalpy and entropy of activation for hydrolysis of ethyl cinnamate in mixed solvent system. Journal of Physical Chemistry& Bio physics. Vol-7, issue-1.1000238.

12. Singh AK. Kinetics and Solvent Effect in Hydrolysis of Ethyl Cinnamate in Water-Methanol Mixture. Journal of Physical Chemistry& Bio physics. Volume-7 issue3.1000252.

13. R.T. Singh, V. K. Lal, ARJ Phys. Sci; 2015, 18 Nos. (1-2), 75-86.

14. N. Kumar, NIRJ Sci. 2016 (June), 20, 51-64.

15. R. K. Wolford, J. Phys. Chem., 1964, 67, 3392.

16. Robertson RE. A survey of thermodynamic parameter for solvolysis in water, Prog. Phy.Org. chem. 4, 1967, pp. 213.

17. Robertson RE et al. A survey of thermodynamic parameter for solvolysis of water. Canadian journal of chemistry. 1959; 37(4):803-824.

18. Arjuman Bano et al. A kinetic study of dipolar protic solvent in alkaline hydrolysis of ethyl nicotinate in water ethanol media-A solvent effect. Journal of ultrachemistry. 2017; 13(6):145-150.

19. R. N. Singh et. al.: A kinetics study on the solvolysis of heavier tatly acid Ester in aquo-n-propanol solvent system, Napier. Ind. Adv. Resch. J. Sc., 12, 2013, 6771.