
SOLVENT-EFFECT OF A DIPOLAR. PROTIC SOLVENT-SYSTEMS ON THE MEDICINAL POTENTIAL OF HEXAMOATES

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Introduction: Various researchers¹⁻³ have reported about the solvent effect on the solvolysis of simple esters and amides but the study of the effect of solvent on the biochemical and medicinal potential of esters having longer carbon chain has not been paid adequate attention so far, So it was thought essential to study the solvent effect on the alkali catalysed solvolysis of the propyl hexanoate (having longer chain) as it seems fruitful from biochemical as well as medicinal points of views, in the best interest of human beings.

Experimental : The kinetics of alkali catalysed solvolysis of propyl hexanoate was studied in water-ethanol (water-EtOH) media having varying composition of the reactant media, separately prepared by adding 30 to 80% of EtOH in it. The reaction mixture was prepared such that its strength in terms of ester as well as alkali were kept 0.05M and 0.1M respectively. The temperatures of the reaction were varied from 20 to 40°C. The reaction was found to follow the second order kinetic equation and the evaluated values of specific rate constants are recorded in Table-I. The evaluated values of Iso-composition activation energy (E_C) and Iso-dielectric activation energy (E_D) respectively in Table - II and III. From the slopes of the plots of $\log k$ values versus $\log [H_2O]$ values (their values recorded in Table - IV), the evaluated values of no. of water molecules associated with the activated complex have been inserted in Table -V. The consolidated values of the thermodynamic activation parameters have been tabulated in Table -VI.

Results and Discussion:

Solvent Effect on the Specific Rate Constants of the Reaction: From Table-I, it is clear that specific rate constant values of the reaction go on decreasing with increasing EtOH

content of the reaction media. From the plots of $\log k$ with mole % of organic co-solvent it is observed that the plot follows a sharp decreasing trend upto 27.50 mole % EtOH at all temperatures. After 27.50 mole % of EtOH in the reaction media, the depletion in the rate becomes slow at all the temperatures. However, sharpness in the depletion of the rate becomes greater with increasing temperature of the reaction. The trend of variation in the values of specific rate constant may be discussed in light of the Hughes and Ingold⁴ Theory. According to the theory, increase in dielectric constant values of the reaction media results in increase in the rate when there is concentration of charges on the transition state and causes a decrease in the rate when there is diffusion or destruction of charges on the transition state. This fact is true that there is decrease in the dielectric constant values of the aquo-EtOH mixture with the gradual addition of organic co-solvent. In the alkali catalysed hydrolysis of propyl hexanoate, due to participation of OH^- ion (Negative ion), the negative charge is dispersed on the larger area of the transition state, so in water-EtOH mixtures, the rate of the reaction should decrease with increase in the dielectric constant of the media according to the Hughes and Ingold theory. But, in our case, the specific rate constant values were found obeying decreasing trend with decrease in the dielectric constant values of the medium or with the addition of organic co-solvent (EtOH) in the reaction mixture, the following factors seem to have been responsible:

- (i) lowering of the bulk dielectric constant of the medium after adding more and more EtOH to it,
- (ii) decreasing the polarity of the medium as changing from polar water to less polar water EtOH medium.

Both of the above noted factors are found to be responsible for depletion in the rate throughout the region of the water-EtOH media in which the kinetics of the reaction were studied. After all the depletion in the rate of reaction may partly be attributed to the dielectric effect and partly due to solvation effect (solvent-solute and solvent-solvent interactions) which are simultaneously operative in case of the hydrolysis of propyl hexanoate in water-EtOH media in the similar manner as reported recently by Singh & Singh et al.⁵ and Singh & Hafizee et al.⁶

Table - 1

Specific rate constant values of Alkali catalysed hydrolysis of Propyl hexanoate in water-EtOH media
 $k \times 10^3$ in (dm)³ mole⁻¹ min⁻¹

Temp in °C	% of EtOH (v/v)					
	30%	40%	50%	60%	70%	80%
20°C	81.18	73.81	67.87	63.62	58.78	53.47
25°C	120.25	106.64	95.96	86.62	76.23	67.03
30°C	170.33	156.24	134.93	117.38	102.14	79.45
35°C	269.96	220.60	186.12	151.69	123.00	98.42
40°C	370.42	310.03	256.09	200.54	162.26	121.14

Table - II

Evaluated values of Iso-composition Activation Energy (E_c or E_{exp}) of the reaction in water-EtOH media.

% of EtOH (v/v)	30%	40%	50%	60%	70%	80%
E_c value in kJ/mol	58.59	55.46	50.76	45.17	39.17	32.06

Table - III

Evaluated values of Iso-Dielectric Activation Energy (E_D) of the reaction at Desired "D" values of the water-EtOH media.

D values	D = 35	D = 40	D = 45	D = 50	D = 55	D = 60
E_D value in kJ/mol	42.22	46.49	51.09	55.63	59.84	65.51

Table -IV

Variation of log k values of the reaction at different temperatures with mol% of DMF in water-DMF media.

% of EtOH (v/v)	% of H ₂ O	log [H ₂ O]	3 + log k values				
			20°C	25°C	30°C	35°C	40°C
30%	70%	1.5898	1.9094	2.0801	2.2313	2.4301	2.5687
40%	60%	1.5229	1.8681	2.0279	2.1938	2.3436	2.4918
50%	50%	1.4437	1.8317	1.9821	2.1301	2.2698	2.4048
60%	40%	1.3468	1.8036	1.9376	2.0696	2.1978	2.30022
70%	30%	1.2218	1.7692	1.8821	2.0092	2.0899	2.2102
80%	20%	1.0458	1.7281	1.8263	1.9001	1.9931	2.0833

Table - V

Values of the slopes of the plots of log k versus log [H₂O] at different temperatures

Temperature in °C	Slope - I Where log[H ₂ O] value is below 1.375	Slope - II Where log[H ₂ O] value is above 1.375
20°C	0.257	0.476
25°C	0.381	0.615
30°C	0.569	0.678
35°C	0.630	1.078
40°C	0.738	1.137

Effect of solvent on Iso-composition Activation Energy (E_C or E_{exp}) of the reaction:

The values of iso-composition activation energy (E_{exp} or E_C) of the reaction have been evaluated from the Arrhenius plots of log values of the reaction against $10^3/T$. and the numerical values of E_C of the reaction have been enlisted in Table - II. From Table - II, it is clear that there is depletion in the E_{exp} values with increase in the concentration of EtOH in the reaction media. The E_{exp} value decrease from 58.59 kJ/mol to 32.06 kJ/mol. It has been established that changes in the values of activation energy are obviously noticeable only when the solvation changes take place either in the initial state level or at the transition state level or at both the levels. The decrease in the activation energy of the reaction with decrease in the specific rate constant values may seem to be quite natural. The following three possibilities may be held responsible for depletion in the values of E_{exp} .

- (i) The transition state is more solvated than the initial state,
- (ii) The transition state is less desolvated than the initial state, and
- (iii) The transition state is solvated and the in initial state is desolvated.

Out of these three factors, the third seems to be applicable in our case as this factor is supported by the decrease in the values of entropies of activation as depicted ahead in Table - VI. This conclusion has also been supported by recent works of Singh & Hafizee et al⁶., Singh & Perween⁷ and Monalisa & Singh et al.⁸

Solvent Effect on Iso-dielectric Activation Energy (E_D) of the Reaction:

The values of Iso-dielectric activation energy (E_D) of the reaction were evaluated from the slopes of the Arrhenius plots of interpolated values of $\log K_D$ (obtained from the plots of $\log k$ values against D values of the reaction media at different temperatures) and are recorded in Table - III. From the E_D values enlisted in Table - III, it is obvious that they go on enhancing from 42.22 kJ/mol to 65.51 kJ/mol with increasing D values of the reaction at $D = 35$ and $D = 60$ respectively. Such enhancement in E_D values of the reaction with increase in D values of the reaction media is also in accordance with the depletion in E_C values of the reaction with increasing concentration of the organic content (EtOH) of the reaction media as

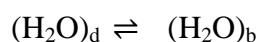
the D values of the reaction media decreases with increasing concentration of EtOH to it. However, these findings and inferences are found in support of the past view of Elsemongy et al.⁹, Wolford¹⁰ and also of the recent reports of Singh & Singh.¹¹

Effect of concentration of water [H₂O] of the reaction media on the Rate and Mechanism of the reaction: The effect of water concentration [H₂O] of the water-EtOH mixture, on the rate and mechanism of alkali catalysed hydrolysis of propyl hexanoate has been studied. For this, the number of water molecules associated with the activated complex was determined by plotting log k against log[H₂O] according to the relation proposed by Robertson.¹⁵

$$\log k = \log k' + n \log [\text{H}_2\text{O}]$$

Here 'n' is the solvation number which tells about the criterion for studying about the mechanism of the reaction. The log k of the reaction and log[H₂O] values of the reaction media have been incorporated in Table -IV. The values of slopes of the plots of log k versus log [H₂O] at all the temperatures are noted in Table -V. From the noted values of the slopes in Table -V, it may be seen that with rise in temperature of the reaction from 20 to 40°C, the values of slopes go on increasing from 0.257 to 0.738 when log [H₂O] value is below 1.375 which corresponds to 42.70% of water in water-EtOH media. Similarly, above log [H₂O] value 1.375 (water concentration 42.70%), number of water molecules associated with the activated complex increases from 0.476 to 1.137 with rise in temperature of the reaction. Overall, it may be inferred that number of water molecules involved with the transition state increases from 0.257 to 1.137 with rise in the temperature of the reaction from 20 to 40°C.

These observations may be attributed to the fact that with addition of EtOH in the reaction media, the equilibrium of the water components of the reaction media shifts from its dense form to its bulky form with the rise of temperature.



Finally, it is inferred that with rise of temperature, the number of water molecules associated with the activated complex increases as the proportion of bulky form of water increases with increase in EtOH content in the water-EtOH mixture and it explains that when

EtOH added to water, the mechanistic path of the reaction is changed from bimolecular to unimolecular in the similar way as observed by Parker and Tomlinson¹³ and recently by Singh & Perween⁷, Monalisa & Singh et al.⁸ and Kumar & Singh.¹⁴

Solvent Effect on the Thermodynamic Activation Parameters of the Reaction:

The thermodynamic activation parameters such as enthalpy of activation ΔH^* , entropy of activation ΔS^* and free energy of activation ΔG^* are supposed to be better indicators of the solvent effects displayed by the solvent on the solvolysis reactions. These thermodynamic activation parameters have been evaluated with the help of Wynne Jones and Eyring¹⁵ equation. The values of all these three thermodynamic parameters i.e. ΔH^* , ΔS^* and ΔG^* at different mol% of the organic component of the reaction media have been synchronized in Table- VI. The variation in ΔH^* , ΔG^* and ΔS^* with mol % of the organic component of the ster-EtOH mixtures may be seen with their plots against mol % of EtOH in the reaction media. On careful observation of the data, it is found that ΔG^* value increase from 89.03 kJ/mol to 90.96 kJ/mol with change of proportion of EtOH from 30 % to 80% (v/v) at 30°C. Though the enhancement is not very large, however it cannot be overlooked rather it must be taken into consideration. A similar variation in ΔG^* values with increasing mole % of organic co-solvent has also been reported recently by Singh & Hafizee⁶ and Monalisa & Singh et al.⁸ This gradual non-linear increase in ΔG^* values with increase in mole % of the organic component in the reaction media is indicative of solvation or desolvation of reactants as explained by Absolute Reaction Rate Theory.¹⁶ So far as the variation in ΔH^* and ΔS^* are concerned, it is clear from Table - VI that both of them decrease with increasing mole % of EtOH in the reaction media. However, on perusal of the values recorded in Table -VI, it is interestingly observed that out of these three thermodynamic parameters of the reaction namely ΔG^* , ΔH^* and ΔS^* , ΔH^* and ΔS^* are found to decreasing simultaneously with increase in mole % of EtOH of the reaction media.

According to the relation

$$\Delta G^* = \Delta H^* - T\Delta S^*$$

it can be easily concluded that increase in ΔG^* values with simultaneous depletion found in it can be easily concluded that increase in ΔG^* values with simultaneous depletion found in ΔH^* and ΔS^* values is only possible when the extent of depletion in ΔS^* values greater than that of ΔH^* . The regular depletion to the greater extent in ΔS^* values in comparison to the ΔH^* values clearly indicates that the alkali catalysed hydrolysis of propyl hexanoate in water-EtOH media is entropy controlled and enthalpy stimulating. Moreover non linearity in ΔH^* and ΔS^* curves give information of the fact that specific solvation is taking place in water-EtOH systems as reported by Saville et al.¹⁷ and it also indicates that the random distributions of the components are not acceptable. The similar non-linear variations in ΔH^* and ΔS^* values with increasing mol % of the organic component in the reaction media have also been reported by Tommila et al.¹⁸ and by Singh & Singh^{19,20}.

Verification of Iso-kinetic Relationship and Solvent Effect on Solvent-Solute Interaction:

Barclay and Butler²¹ have developed an iso-kinetic relationship between enthalpy of activation ΔH^* and entropy of activation ΔS^* as follows:

$$\delta_m(\Delta H^*) = \beta \delta_m(\Delta S^*)$$

where β is a constant called iso-kinetic temperature. Leffler²² has pointed out that plot of ΔH^* against ΔS^* results in a straight line and the slope of the line gives the values of iso-kinetic temperature. He pointed out that in many solvolysis reactions, the values of slope of plots of ΔH^* versus ΔS^* come in between 300 and 400 and this foretells about the considerably strong interaction between solvent and solute of the reaction mixture. In the present study also, plots of ΔH^* versus ΔS^* , which is conformity with Barclay-Butler relationship. The numerical value of the slope of the straight line is found to be $281.86 \approx 282$. Thus in light of Leffler's guidelines, from the value of the slope which is less than 300, it can easily be concluded that there is appreciable change in the structure of the reactant or in the solvent or in both the reactant and the solvent due to comparatively weaker interaction between solvent and solute present in the reaction mixture (water-EtOH media) in the similar way as reported by Leffler²². The structural changes with increasing proportion of the EtOH in water-EtOH

solvent system are responsible for the decrease in the specific rate constant values. However, these findings and conclusions have also been supported recently by Ananl & Singh et al²³ and Sushma & singh²⁴.

Table - VI

**Consolidated Values of Thermodynamic Activation Parameters (ΔH^* , ΔG^* and ΔS^*),
of the reaction, in water-EtOH system at different temperatures
 ΔH^* and ΔG^* in kJ/mol, ΔS^* in J/K/mol**

% of EtOH (v/v)	Mole % of EtOH	ΔH^* in kJ/mol	20°C		25°C		30°C		35°C		40°C	
			ΔG^*	ΔS^*	ΔG^*	ΔS^*	ΔG^*	ΔS^*	ΔG^*	ΔS^*	ΔG^*	ΔS^*
30%	11.69	55.91	87.82	-108.90	88.39	-108.97	89.03	-109.31	89.37	-108.64	90.03	-109.02
40%	17.07	52.96	88.05	-119.75	88.68	-119.86	89.25	-119.76	89.88	-119.87	90.50	-119.91
50%	23.59	48.13	88.26	-136.94	88.95	-136.95	89.62	-136.92	90.32	-136.97	91.00	-136.94
60%	31.06	42.98	88.41	-155.05	89.20	-155.09	89.97	-155.08	90.74	-155.06	91.63	-155.43
70%	41.87	36.59	88.61	-177.54	89.52	-177.61	90.32	-177.34	91.38	-177.90	92.18	-177.62
80%	55.85	29.53	88.84	-202.40	89.83	-202.35	90.96	-202.71	91.95	-202.65	92.94	-202.59

References

- 1.Elsemongy, M.M. : Z. Physik Chem.(Neue Folge), **94**, 1, 1971
- 2.Singh, Lallan, Singh, R.T., and Jha, R.C. : J. Indian Chem.Soc., **57**, 1089-1091, 1980
- 3.Singh, Lallan, Gupta A K, Singh,R.T : React . Kinett Catal Lett **24**, No(1-2), 161-165, 1984
4. Hughes E.D. and Ingold C.K. : J. Chem Soc. **225**, 244, 1935
5. Singh, R.T., Kumar,S., Singh,D. and Singh, R.I. : ARJ Phy. Sci. **16**, No. (1-2), 129-137,2013
6. Singh,R.T., Navendu, K.S., Henry, W. and Hafizee, N.K. : NIRJ Sci., **14**, 53-61,2014
7. Singh, RT., Singh, A.K., Kumari V.& Perween, M. :ARJ Phy. Sci. **15**, Nos. (1-2), 151-161, 2012
8. Monalisa, Singh, R.N., Sudhansu, N.S. and Singh, R.T. : NIRJ Sci. **12**, 89-99, 2013
9. Elsemongy, Moussa,M.M., Elamayan, Abu, M.S. : Z. Physik Chem. (Neue Folge), **95**, 215, 1975
10. Wolford, R.K. : J. Phys. Chem. **68**, 3392, 1964
11. Singh, R.T., Singh, P.K., Singh, S.M.& Singh, U.C.: ARJ Phy. Sci. **15**, No.(1-2), 129-139, 2012
12. Robertson, R.E. : Prog. Phy. Org., Chem. 4, 213, 1967.
13. Parker, A.J. & Tomilinson, D.J. : Trans. Faradey. Soc. 67, 1302, 1971
14. Kumar, N, and Singh, R.T.: NIRJ. Sci., 15, 39-46, 2014
15. Wynne-Jones W.F.K. and Eyring, H. : J. Chem. Phys., **3**, 492, 1953
16. Glasstone, S., Laidler, K.J. and Eyring, H. : "The Theory of Rate Process" McGraw Hill, New York, 1941
17. Saville, B.J.and Husdan, R.F. : J. Chem. Soc., 4114, 1955
18. Tomilla, E., and Mevikallio, E. : Somun Kemi. 26B, 79, 1953
19. Singh, RT., Upadhyay, O.P., Radha, B. and Singh, P. : ARJ Phy. Sci. **16**, 139-147, 2013
20. Singh, R.N., Smriti, Kumar, S. and Singh, R.T. :NIRJ Sci. **12**, 67-76, 2013
21. Barclay, I.M, and Butler, J.A.V. : Trans. Faraday Soc. **34**, 1445, 1938

22. Leffler, J.E. : J. Org. Chem., **20**, 1201, 1955

23. K. Anant and Singh RT : NIRJ Sci **27**, (II) 1-12, 2018(March)

24. K. Sushma, Ranjan RK and Singh RT : IJSM,**7**, No(2), 147-162, 2018(Feb).