A Comprehensive kinetic study of the solvent Effect of Aquo-protic Solvent systems on the Medicinal Potential of Propyl Valerate

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ABSTRACT

The Hydrolysis products of the ester valerate is valeric acid and its medicinal and pharmaceutical properties depends on its extensive properties and they are evaluated by studying the catalyzed hydrolysis of valerate ester.

Hence in order to highlight the medicinal potential of valeric acid the kinetics of alkali catalyzed hydrolysis of higher valerate i.e., propyl valerate has been studied in aquo-protic solvents (aquo-ethanol) reaction media which has been found to affect the extensive properties of the reaction quantitatively.

The specific rate constants of the reaction were found decreasing with increasing concentration of the protic organic content (Ethanol) of the media. It is inferred that dielectric effect and the solvation changes are the causes of depletion in the rate of the reaction.

The Iso-composition activation energy (E_C) and the Iso-dielectric activation energy (E_D) of the reaction were found to increase and decrease respectively and from this, it is inferred that the transition state of the reaction is desolvated and its initial state is solvated.

From the evaluated values of iso-kinetic temperature of the reaction which comes to be 320.0, it is concluded that the Barclay-Butler rule is obeyed by the reaction and there is strong solvent-solute interaction in presence of ethanol in the reaction media.

INTRODUCTION :

The Kinetics of alkali catalyzed hydrolysis of propyl valerate in aquo-ethanol media has been planned to be carried out, as this reaction is very useful from commercial as well as the medicinal points of views and also because the study has not been paid adequate attention by the researchers and kineticists up till now.

The solvolysis of the said ester has been studied in aquo-ethanol media having varying concentration of ethanol from 20-80% (v/v) and at five different temperatures i.e., 20, 25, 30, 35 and 40^oC.

Experimental & Calculation :

Export quality fo propyl valerate ester of USSR make and Merck grade of ethyl alcohol were taken into use. The kinetics of alkali catalyzed hydrolysis of propyl valerate were studied using earlier reported process [1,2] keeping the strength of alkali and ester as 0.1M and 0.05M respectively. The concentration of the organic protic solvent ethanol was varied from 20 to 80% (v/v) and hydrolysis was carried out at five different temperatures at 20, 25, 30, 35 and 40^oC. The reaction was found to follow second order kinetic equation and the evaluated values of the specific rate constants were enlisted in Table-I. The evaluated values of iso-composition activation energy (E_C) and iso-dielectric activation energy (E_D) have been recorded respectively in Table-II and III. From the slopes of the plots of log k values versus log $[H_2O]$(recorded in Table-IV), the evaluated values of number of water molecules associated with the activated complex of the reaction have been tabulated in Table-V. The three thermodynamic activation parameters namely ΔH^*, ΔG^* and ΔS^* were calculated by applying Wynne-Jones and Eyring equation[3] and their values are synchronized in Table-VI.

Results and Discussion:

Solvent Effect on the Rate of Reaction:

In the clear from Table-I that the specific rate constant values of the reaction decrease with increasing proportion of ethanol in the reaction media. On plotting log k values against mole % of ethanol shown in fig. 1 it is found that rates of reaction go on depleting with gradual addition of ethanol in the reaction media. The depletion in the rate follows smooth depleting path. From the plots of log k versus mole % of ethanol in the reaction media, two inter secting straight lines having different values of slopes are obtained. The decrease in the rate with increasing mole % of ethanol at all the five temperatures are found to follow deep depletion path up to 21.35 mole % of the ethanol in the reaction media and after its 21.35 mole % in the reaction media, the rate of depletion becomes slow, following shallow path. That sharpness in the depletion of the rate becomes slow with increase in temperate of the reaction. This decreasing trend in the values of the rate constants needs to be discussed in the light of Hughes and Ingold[4] predictions and the theory of Laidler and Landskroener[5]. The values of dielectric constant of the reaction media go on decreasing with gradual addition of ethanol. So these findings are fully in accordance with the qualitative prediction of Hughes and Ingold[4].

However, these findings are also in agreement with the qualitative prediction and views of Singh & Jha et.al.[6,7] and with recent reports of Kavita & Singh et.al.[8] and Atulit Singh[9], who predicted that the rate of ion dipolar reaction decreases partly with decrease in the dielectric constant values of the reaction media and partly due to the solvation changes taking place in the reaction media.

Solvent effect on the Iso-composition Activation energy (E_C) of the reaction:

The values of Iso-composition activation energy (E_C) of the reaction were evaluated from the slopes of Arrhenius plots of log k values of the reaction against $10^3/T$ and have been tabulated in Table-II. The plots of log k versus $10^3/T$ have been shown in Fig.2.

From Table-II, it is obvious that E_C values go on increasing from 100.98 kJ/mol to 134.28 kJ/mol with increase in concentration of ethanol from 20 to 80% (v/v) in reaction media. This change is probably due to solvation changes taking place either at initial state level or at the transition state level or at the level of both the states. Considering the extent of solvation to be a dominant factor. The following three factors seem to be responsible for increase in E_C values with gradual addition of ethanol in the reaction media:

(i) The transition state is desolvated more than initial state

(ii) The initial state is solvated more than the transition state, and

(iii) The initial state is solvated and the transition state is desolvated,

The transition state being large anion (ester +OH^-) not available more for solvation by ethanol molecule than the initial state, so the third factor seems to be operative in this case and it also gets support when the values of entropy of activation (ΔS^*) and enthalpy of activation (ΔH^*) go on increasing with increasing concentration of ethanol as shown in Table-

VI. Such observations and inferences have been found in support of earlier report by Jha & Singh et.al.[10] and also in support of recent report by Zeba & Singh et.al.[11].

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

On perusal of the data of Table-III, it is found that iso-dielectric energy (E_D) values of the reaction are decreasing from 130.76 kJ/mol to 103.30 kJ/mol with increase in dielectric constant values of the reaction media from D=35 to D=65 respectively. Since D values of the aquo-ethanol reaction media go on decreasing with gradual addition of ethanol to it, hence it may also be concluded that like E_C values, E_D values are also increasing with decrease in D values of the reaction media or with adding more and more ethanol to it. Thus, it also may be opined that E_C and E_D values of the solvolysis reactions are complimentary to each other.

Such findings and their interpretations have been found in support of the past views of Elsemongy et.al.[12], Wolford[13] and are also found in favour of the recent report of Anant[14] and Sushma[15].

Effect of Solvent on the Solvation number and on the Mechanistic pathways of the reaction:

The solvation number i.e., the number of water molecules involved in the formation of the activated complex of the reaction were evaluated from the slopes of the plots of log k values of rate constants against log $[H_2O]$ values of the reaction media by using Robertson[16] equation which is –

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

Where 'n' is the solvation number.

The log k and log $[H_2O]$ values are in listed in Table-IV and their plots are shown in Fig.3 and the numerical values of the slopes of the plots have been enlisted in the Table-V.

Robertson et.al.[17] have established that the numerical value of solvation number 'n' i.e., the number of water molecules associated with the activated complex in its formation are fairly high for reaction following unimolecular mechanistic pathway and are low for reaction following bimolecular mechanistic pathway.

From the evaluated values of slopes as recorded in Table-V, it is clear that before log $[H_2O]$ value 1.456 which corresponds to 52.50 of water concentration in the reaction media. Their values are decreasing from 0.717 to 0.226 with rise in temperature of the reaction from

20 to 40^{o}C. Similarly, after log [H_2O] values 1.465 i.e., above 52.50% of water in the reaction media, the numerical values of the slopes i.e., the number of water molecules associated with the activated complex in its formation decrease from 1.370 to 0.355 with increase in temperature from 20 to 40^{o}C.

Overall, it may be concluded that number of water molecules associated with the activated complex of the reaction in the formation decrease from 1.37 to 0.226.

Thus, on the guidelines of Robertson et.al.[17], it may be inferred that with rise in temperature of the reaction, the mechanistic pathways of the reaction is changed from unimolecular to bimolecular in presence of ethanol in the reaction media.

About the change in the structure of water in presence of ethanol and with rise in temperature of the reaction, water components of the reaction media change its structure from its bulky form to dense form at equilibrium.

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

Such observations and inferences have been found in support of earlier report by Singh & Mishra et.al.[18] and also with the recently reported findings by Anjana & Singh et.al.[19].

Solvent effect on Iso-kinetic Temperate of the Reaction and Solvent Solute Interaction in the Reaction Media:

This reaction is found to obey Barclay and Butler[21] rule and straight line is obtained when ΔH^* values of the reaction is plotted against ΔS^* as shown in Fig.-4 and form their values tabulated in Table-VI.

The Barclay and Butler equation is –

$$\delta m(\Delta H^*) \quad = \quad \beta \, \delta m(\Delta S^*)$$

It is a relation between enthalpy (ΔH^*) and entropy (ΔS^*) of activation values of the reaction and 'β' is called iso-kinetic temperature of the relation which is also called Leffer-Grunwald solvent stabilizer operator[22]. From the values of slope of the plot, the values of Iso-kinetic temperature was evaluated which came to be 319.19 ≅ 319.0

In the light of Leffler[23] guidelines, from the values of iso-kinetic temperature which is greater than 300, it is inferred that there is a considerable change in the structure of the reactant or in the solvent or in both the reactant and the solvent due to appreciably strong interaction between the solvent and the solute present in the reaction media. The structural changes with increasing proportion of ethanol in aquo-ethanol reaction media are responsible for the depletion observed in the values of the specific rate constant of the reaction.

In recent years Ajeet & Singh et.al.[24] and Ojha &Singh et.al.[25] have also reported similar conclusions and their interpretations about the solvent-solute interaction in the reaction media.

Specific rate constant values of Alkali catalysed hydrolysis of propyl valerate inAquo-Ethanol media

k x 10^3 in (dm)3 mole^{-1} min^{-1}

Temp in ºC	% of Ethanol (v/v)						
	20%	30%	40%	50%	60%	70%	80%
20°C	75.33	63.55	51.00	43.63	34.77	27.23	21.99
25°C	147.79	128.94	109.37	93.28	79.79	65.86	54.39
30°C	293.39	264.36	232.92	208.88	183.74	158.45	134.83
35°C	556.39	508.28	466.87	432.71	396.10	354.16	313.83
40°C	1049.78	996.32	943.84	895.57	843.72	789.95	732.66

Table - II

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

% of Ethanol (v/v)	20%	30%	40%	50%	60%	70%	80%
E_C valuesin k/J/mol	100.98	104.97	111.74	115.75	121.20	127.64	134.28

Table – III

Evaluated values of Iso-Dielectric Activation Energy (E_D) of the reaction at Different-Desired 'D' values of water-Ethanol media.

D values of Aquo-Ethanol media	D=35	D=40	D=45	D=50	D=60	D=65
E_C valuesin k/J/mol	130.76	124.23	121.66	118.18	113.05	103.30

Table - IV

Variation of log k values of the reaction with log [H_2O] values of water-Ethanol media at different temperature.

% of Ethanol (v/v)	% of H_2O	log [H_2O]	3 + log k values				
			20°C	25°C	30°C	35°C	40°C
20%	80%	1.6478	1.8770	2.1699	2.4682	2.7452	3.0211
30%	70%	1.5898	1.8031	2.1104	2.4221	2.7061	2.8984
40%	60%	1.5229	1.7076	2.0389	2.3672	2.6692	2.9149
50%	50%	1.4437	1.6398	1.9698	2.3199	2.6362	2.9521
60%	40%	1.3468	1.5412	1.9008	2.2642	2.5978	2.9262
70%	30%	1.2218	1.4351	1.8182	2.1999	2.5492	2.8976
80%	20%	1.0458	1.3422	1.7355	2.1298	2.4967	2.8649

Table - V

The Values of the slopes of the plots of log k versus log [H_2O] at different temperatures

Temperature in °C	Slope - I Where log[H_2O] is below 1.465	Slope - II when log[H_2O] is above 1.465
20°C	0.717	1.370
25°C	0.538	1.012
30°C	0.439	0.877
35°C	0.360	0.664
40°C	0.226	0.355

Table – VI

Evaluated Values of ∆H*, ∆G* and ∆S* of the reaction in water-Ethanol media at 30ºC
∆H* and ∆G* in kJ/mol and ∆S* in J/K/mol

% of Ethanol	Mole % of Ethanol	∆H* kJ/mol at 30ºC	∆G* in kJ/mol at at 30ºC	∆S* J/K/mol at 30ºC
20%	07.17	98.46	81.86	54.70
30%	11.69	103.14	82.13	69.34
40%	17.07	109.50	82.44	89.31
50%	23.09	113.95	82.74	103.07
60%	31.06	119.05	83.04	118.84
70%	41.87	125.50	83.41	138.84
80%	55.85	131.30	83.82	156.91

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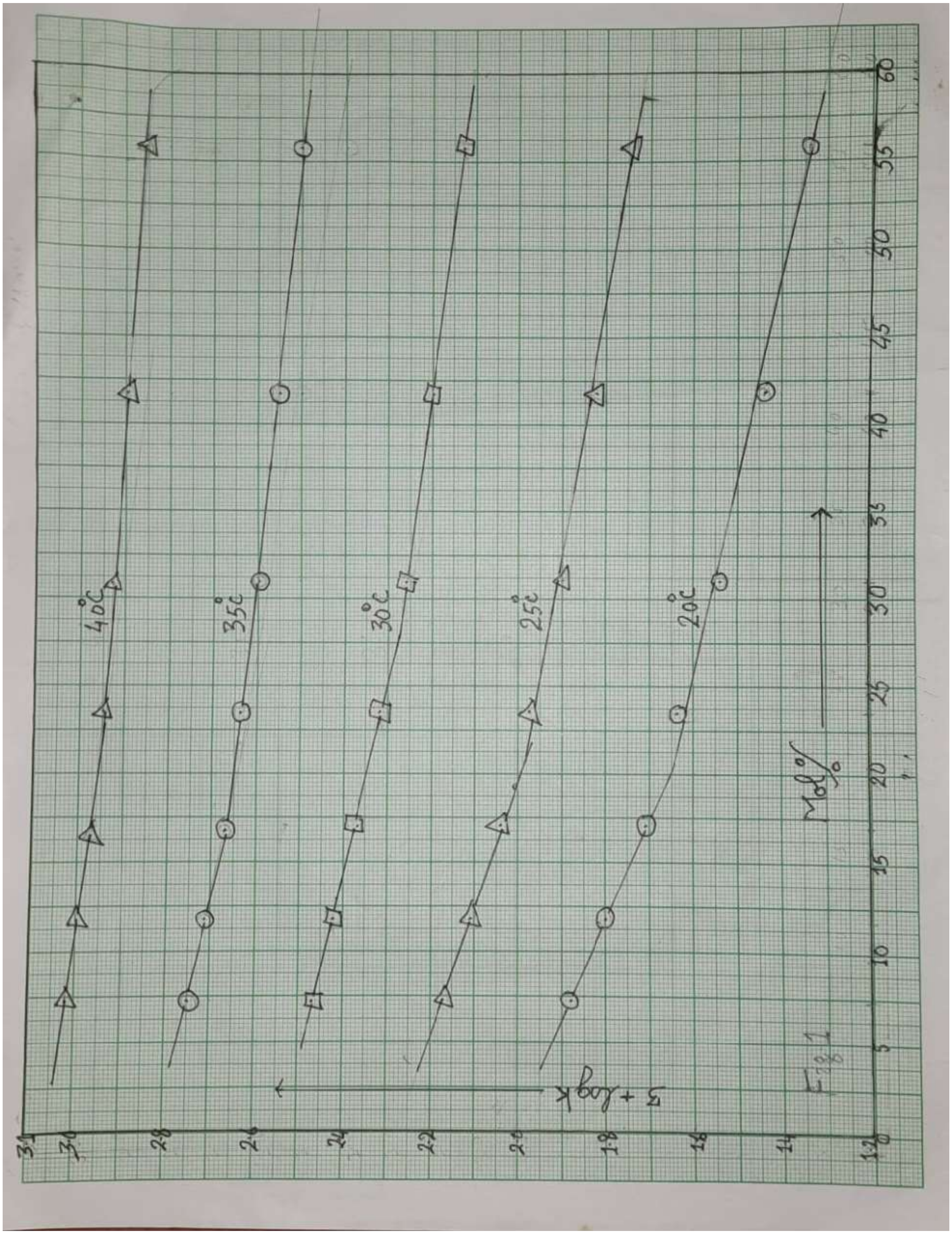
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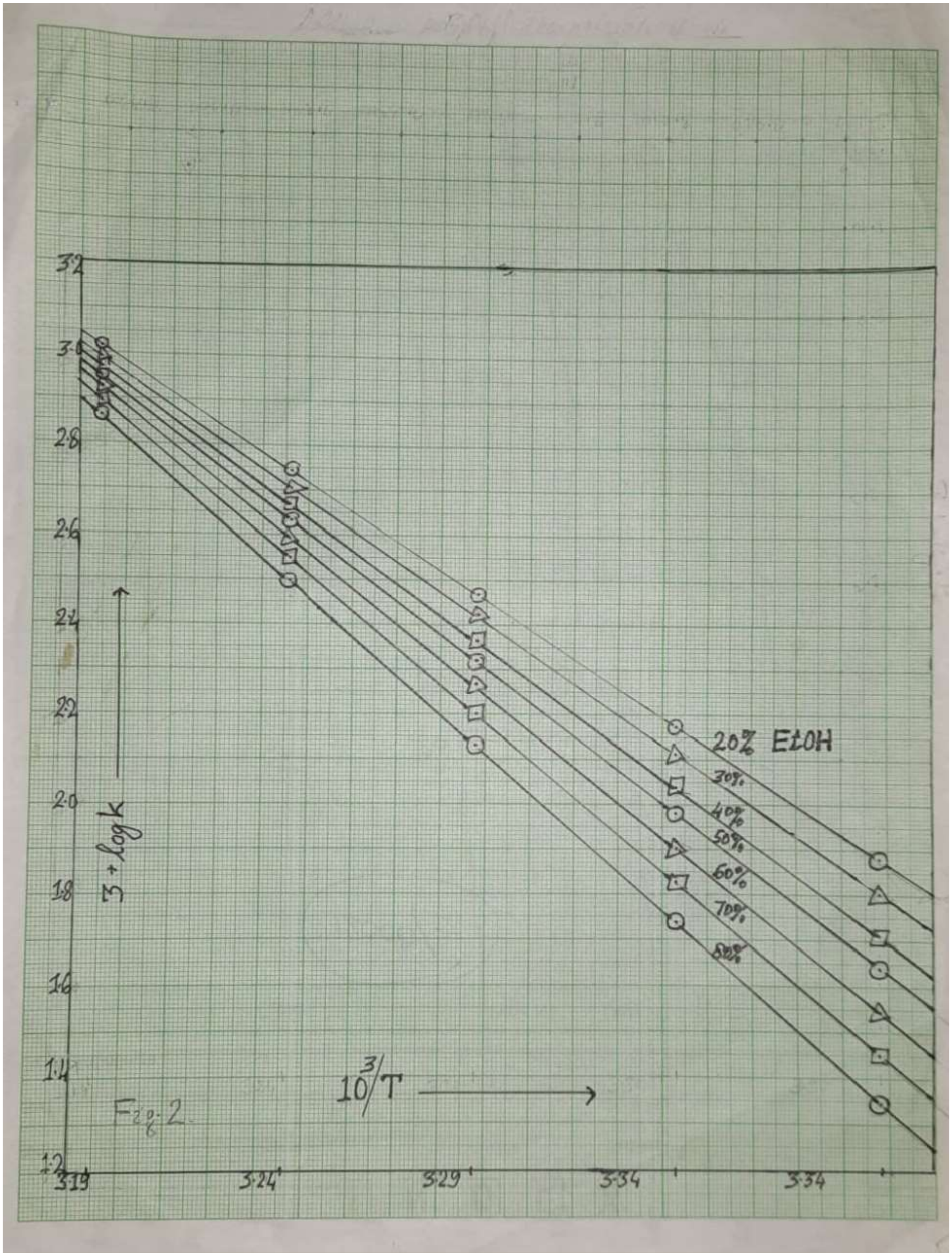
Fig. 1

[13.]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3 + log k
$10^3/T$
Fig. 2
20% EtOH
30%
40%
50%
60%
70%
80%

[14.]

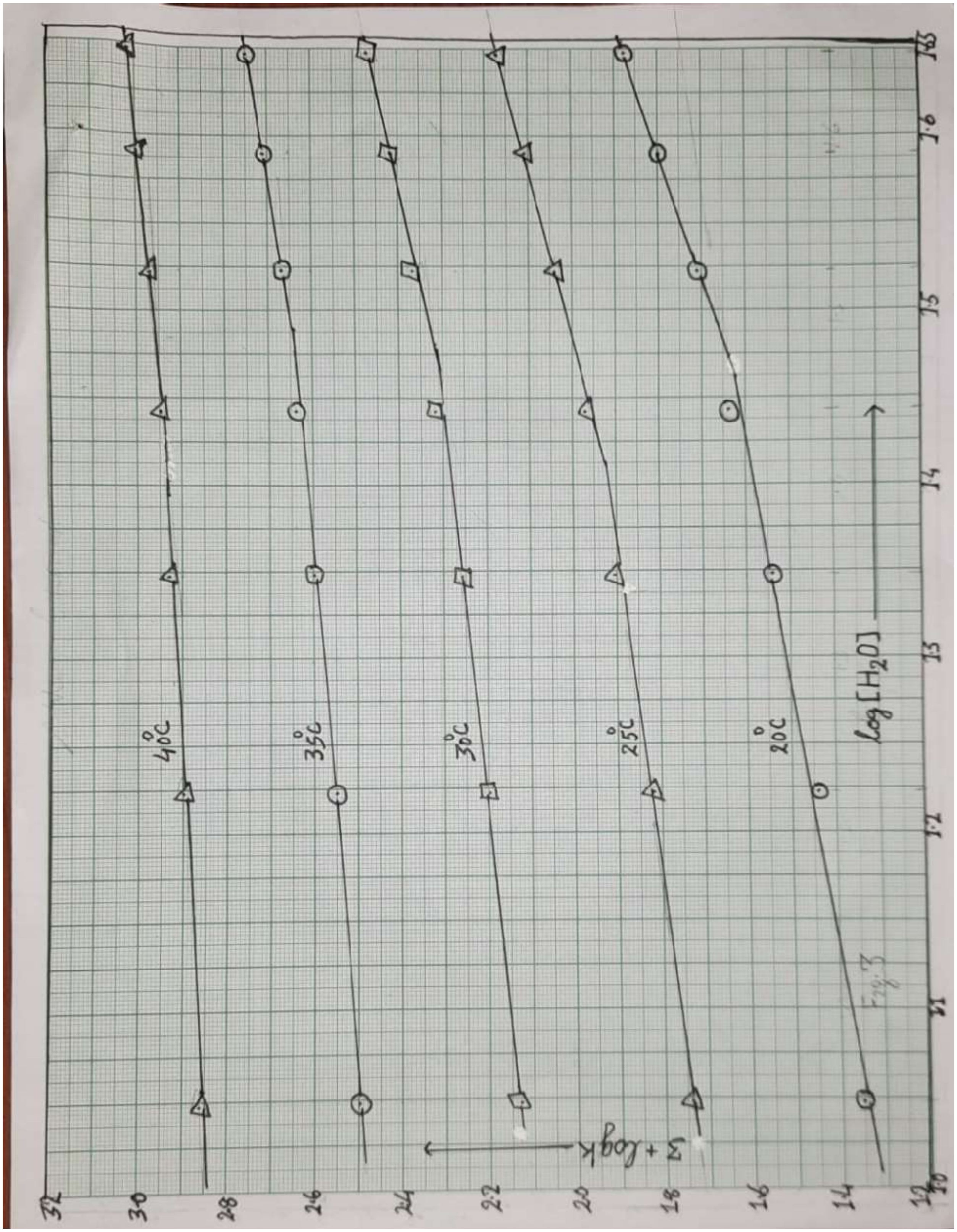
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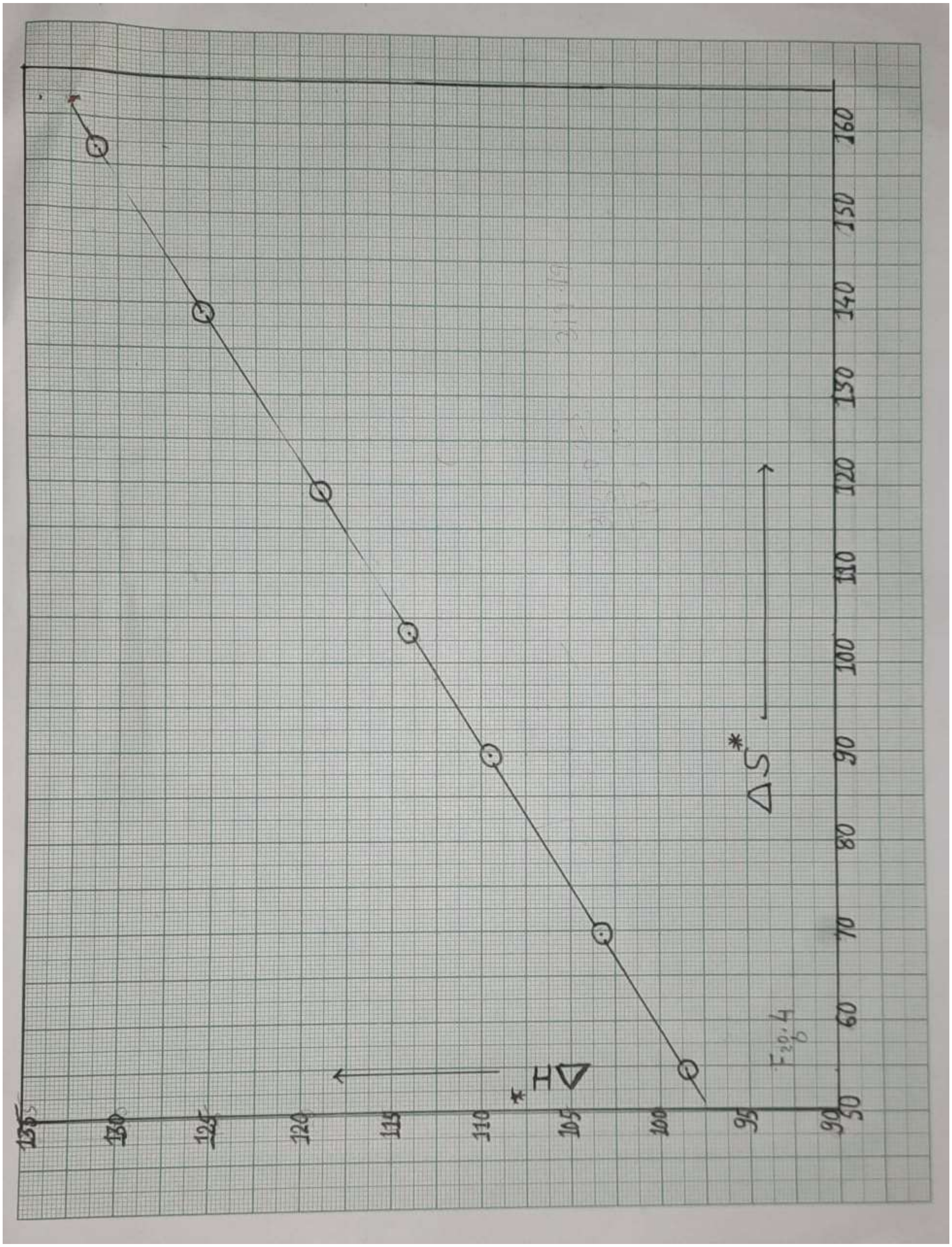
Fig. 3

[15.]


ΔH*
ΔS*
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[16.]