Kinetic Parameters of the Ketoesters and Solvent and Structural Influences

The role of water in regard to rate-determining stage in the hydrolysis of the three keto esters, as the composition of organo-aqueous binary is changed, has been dealt with in the previous chapter. The change in the composition of the medium is inseparably connected with the alteration of the overall macrodielectric constant. Hence, the solvent effect on the mechanism of hydrolysis of the esters can also be, if desired, linked up with the variation of the dielectric constant conceived in the sense of a dielectric continuum.

Besides mechanism, there are other kinetic aspects revealed in these experiments - such as magnitudes and trends of variation of rate constants, activational energies, entropies and free energies - which cannot be totally explained in terms of macrodielectric constant of the solvent, though this constitutes the predominant factor.

We then recall here once again the various influences (vide chapter 2) which are of importance in the hydrolysis of keto esters in binary solvent medium and cumulatively determine the solvent and other effects on kinetics.
1) Macro dielectric constant controlling electrostatic interaction between reactant molecules and general solvation of the reactants.

2) Preferential solvation or solvent sorting as distinct from general solvation.

3) Solute-environment structure.

4) Solvent structural unit.

5) Structural effects of the reactants.

Of the factors enumerated above, (2) and (3) together with general solvation under (1) constitute solute-solvent interaction. The factors (4) and (5) are independently characteristic of the solvent and solute (reactant) respectively.

A – The rate constant - Dielectric constant correlations

The theoretical requirements of the linear variation of log $k_{\text{obs}}$ with the reciprocal of dielectric constants is only partially obeyed in most of the present cases (figs.2.11, 2.12, 2.20, 2.21). There have been some stray cases of complete obedience in the case of hydrolysis of pyruvic ester (figs.2.24 & 2.25). The departure from linearity may originate from two causes:

(a) In building up the different theoretical equations using macro dielectric constant, only the electrostatic
FIG. 224. PLOT OF LOG₁₀ ku₅₅ Vs THE RECIPROCAL OF THE DIELECTRIC CONSTANT

(a) (b) (c) (d) (e)

Water- acetone medium.

Water- diozone medium.
interaction between the reactants has been considered. The general solvation of the reacting species and of the transition states is not reflected in these equations.

(b) The preferential solvation by the higher dielectric component of the medium results in solvent sorting. Even when there is no change in mechanism, this property may result in the departures of points from initial linear behaviour. This property is, perhaps, responsible for the breaks in $\log k_{\text{obs}}$ Vs $\frac{1}{D}$ curves of the hydrolysis of levulinic ester where the mechanism remains the same.

As has been pointed out so often in the literature (loc.cit), this preferential solvation becomes a significant factor to contend with, only when organic component of the medium is relatively high. In the earlier stages of high water content, this preferential solvation does not affect the linearity between $\log k_{\text{obs}}$ Vs $\frac{1}{D}$. When, with the increase of organic component of the medium, this solvent sorting effect is superposed on the macro dielectric constant effect, the nature of $\log k_{\text{obs}}$ Vs $\frac{1}{D}$ curve will be dependent on whether the former effect is too strong or a mild one. If the effect is only weak or just moderate, the deviating points may still lie fairly closely on a second straight line instead of forming a curved tail (vide figs. 22, 23, 24, 25).
The evaluation of the radius of the activated complex has been made by utilising the slope values of \( \log k_{\text{obs}} \) vs \( \frac{1}{D} \) curves for ethyl pyruvate, ethyl acetoacetate and ethyl levulinate and are recorded in tables 3A_1, 3A_2 and 3A_3. In these evaluations, Laidler-Landskroener equation has been used together with their G* values for the transition state complexes in ester hydrolysis. Such use of a common G* value even with different esters has also been made previously. The justification lies in the fact that the radius of the transition state is only an effective value of the spherical cavity (not the total molecule) which represents the reaction zone and contains the distribution of charges. The G* value is, therefore, likely to be within a certain range for the alkaline hydrolysis or for the acidic hydrolysis of all esters if the prevailing mechanism be the same as proposed by Laidler and Landskroener (loc. cit).

**Table - 3A_1**

*Dimension of Transition State Complex in the Acid Hydrolysis of Ethyl Pyruvate.*

<table>
<thead>
<tr>
<th>Water - dioxane</th>
<th>Water - acetone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Temp. ( ^{\circ}C )</strong></td>
<td><em><em>b</em> ( (A^0) )</em>*</td>
</tr>
<tr>
<td>25.</td>
<td>4.50</td>
</tr>
<tr>
<td>30.</td>
<td>4.60</td>
</tr>
<tr>
<td>35.</td>
<td>4.68</td>
</tr>
<tr>
<td>40.</td>
<td>4.62</td>
</tr>
<tr>
<td>45.</td>
<td>4.56</td>
</tr>
</tbody>
</table>
### Table - 3A₂

**Dimension of Transition State Complexes in the Basic Hydrolysis of Ethyl Acetoacetate**

<table>
<thead>
<tr>
<th>Water - dioxane</th>
<th>Water - acetone</th>
</tr>
</thead>
<tbody>
<tr>
<td>**Temp. **°C</td>
<td></td>
</tr>
<tr>
<td>b* (A₀)</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>1.97</td>
</tr>
<tr>
<td>30</td>
<td>1.94</td>
</tr>
<tr>
<td>35</td>
<td>1.94</td>
</tr>
<tr>
<td>40</td>
<td>1.89</td>
</tr>
<tr>
<td>45</td>
<td>1.66</td>
</tr>
</tbody>
</table>

### Table - 3A₃

**Dimension of Transition State Complexes in the Basic Hydrolysis of Ethyl Levulinate**

<table>
<thead>
<tr>
<th>Water - dioxane</th>
<th>Water - acetone</th>
</tr>
</thead>
<tbody>
<tr>
<td>**Temp. **°C</td>
<td></td>
</tr>
<tr>
<td>b* (A₀)</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>1.92</td>
</tr>
<tr>
<td>30</td>
<td>2.0</td>
</tr>
<tr>
<td>35</td>
<td>1.98</td>
</tr>
<tr>
<td>40</td>
<td>1.98</td>
</tr>
<tr>
<td>45</td>
<td>1.98</td>
</tr>
</tbody>
</table>
The radii values for the transition state complex in the hydrolysis of ethyl acetoacetate ($3A_2$) have been calculated from the slopes of the lower straight lines in figs. 2.11 & 2.12. It is here that the prevailing mechanism of hydrolysis has been considered to be identical with that proposed by Laidler and Landskroener (loc. cit.). Similar considerations also apply to the radii values in the hydrolysis of ethyl levulinate and ethyl pyruvate. Except for some peculiarity of a sharp drop at $45^\circ C$ for basic hydrolysis of ethyl acetoacetate, the values are within the acceptable limits and are fairly insensitive towards temperature variations (tables $3A_2$ and $3A_3$).

The magnitudes of the radii evaluated in the acid hydrolysis of ethyl pyruvate are larger as expected and lie, once again, within the acceptable limits.

B-I. Trend of Changes of Activational Energies and Entropies.

It has been mentioned in chapter 2, that the mechanisms of hydrolyses of pyruvic ester, acetoacetic ester and levulinic ester comprise mixed processes.

The average values of entropies of activation, energies of activation (Tables $2A_1 - 2A_3$, $2B_1 - 2B_3$, $2C_1 - 2C_3$) as well as their true split values calculated on the
basis of the operative mechanisms (Tables 2A₄, 2A₅, 2B₇, 2B₈, 2C₆, 2C₇) reveal a very characteristic feature common to all the three. While the rate constants at any particular temperature show a decrease with decrease in dielectric constant (i.e. increase in concentration of the organic component) of the binary medium, energies of activation go on decreasing accompanied by corresponding decrease in entropies of activation. The free energies of activation, however, change in step with the rate constants in opposite sense.

This expected trend of change of free energies of activation in all cases is accountable in terms of the well known compensation effect⁶ i.e. proportionate mutual neutralisation of the consequences of decrease in activational entropy and decrease in activational energies. The linear relation between \( TΔS^* \) and \( ΔH^* \) demanded by this is shown in figs. 2.3 & 2.4.

Confining ourselves now to any particular system, say ethyl acetoacetate, it may be worthwhile to examine the gradual decrease in \( ΔS^* \) and decrease in \( ΔH^* \) values. This is considered in the following two sections.

B-II. Solvent Structural Unit - Vis a Vis \( ΔS^* \) and \( ΔH^* \)

Adequate attention has been drawn to the importance attached by different authors⁷,⁸,⁹ to the organised
solvent structural units of organo-aqueous binaries in the exhibition of maxima and minima of many thermodynamic and kinetic properties. The trend of changes in any kinetic property e.g. energy of activation and the occurrence of the extremum are, according to them, not very dependent on the solute reactant species, but are essentially the property of the solvent. If one examines the changes in $\Delta H_S$ in dioxane-water and acetone-water binaries (Mckelvey, fig.1.1, chapter 1) one notices gradual drop (barring the maximum) from the higher water-content side to the lower water-content side.

A similar situation in the trend of changes in the entropies and energies of activation (without extremum) is observed in the hydrolysis of ethyl acetoacetate (Tables 2B1 - 2B3). On the higher water-content side, the concentrations of the organised structural units are relatively more than those on the lower water-content side. Solvation of the polar transition states would thus entail a prior break-up of the structural units to a certain extent. This would mean that the final drop in $\Delta S^*$ values on the higher water-content side of the binary will not be too large. But on the lower water-content side, the organised solvent structural units being relatively few, the solvation of the transition state complex will not entail much of the break-up
process and this would register sharp decrease in $\Delta S^*$. This interpretation, valid for hydrolysis of ethyl acetoacetate, is in general valid also for the corresponding reactions of ethyl levulinate and ethyl pyruvate.

B-III. Solute – environment Structure Vis a Vis $\Delta S^*$

An alternative qualitative interpretation of the sharp changes in $\Delta S^*$ with increase in organic component may be attempted on the basis which lays stress on the solute-environment structure rather than on the solvent structural units of the previous sections.

The reactant systems of our study consist of dipolar ester molecule, dipolar water molecule and OH$^-$ or H$^+$ ions. The transition state complexes, considered according to the models of Laidler and Landskroener (loc.cit), comprise three (or four) charge centres with an effective radius value $\sim 2\AA$ (Table 3A$_2$ and 3A$_3$) for the basic hydrolyses and $\sim 4.5\AA$ (Table 3A$_1$) for acid hydrolysis. In general, the transition states will be more solvated than the reactants considered together causing a decrease in entropy.

An analogous view namely that a large transition state with dispersed charge distribution will be more solvated in less protic dipolar solvents has also been put forward by Kingsbury$^{11}$. 
One may now recall the structure of the solute-environment (page 23) with three distinct zones 'A', 'B', and 'C' for media with high water and low water contents. The solvent molecules in zone 'B' subjected to different orientational influences of the solute species and of the ice-like structured molecules in 'C' will be in a relatively more orientational disorder. For media of high water content, the zone 'C' will be more ice like and exert a greater orientational influence on solvent molecules in zone 'B', simultaneously with the countering influence emanating from the solute species with the encircled zone 'A'. When the water content is low in the organo aqueous binary, the molecules in zone 'C' will be less ice-like and the 'B' zone molecules will be more and more subjected to the exclusive influence of the solute species encircled by 'A'. The result may be widening of the 'A' zone of immobilised molecules at the cost of narrowing down of the 'B' zone as one passes from a more aquated reacting medium to a medium which is less so. It thus transpires that of the two reacting systems - one binary with higher water-content and the other binary with lower water-content - the latter will have less entropy. And when the more polar transition states (cf. Kingsbury) are formed in the two cases, the squeezing of the 'B' zone the simultaneous expansion of the 'A' zone, become, perhaps more effective in the latter case
to record a sharper drop in the entropy of activation. One additional factor other than the more polar character of the transition state contributing towards reduction in entropy is the decrease in the number of solute species in yielding one transition state complex.

Now since \(-T\Delta S^*\) and \(\Delta H^*\) curves as functions of composition in such organo aqueous binaries form almost a mirror image\(^{12}\) of each other, activational energies go on decreasing. At least, this has happened up to the maximum concentration limit of the organic component used in each of the binaries of our kinetic systems.

C. Structure of the Reactants and its Bearing on Rate Constants.

The influence of the structure of the reacting esters on the relative magnitudes of the rate constants will now be considered briefly. The three esters contain the keto group in the \(\alpha\), \(\beta\) and \(\gamma\) positions respectively. Since the dipolar direct electrostatic\(^{13}\) field effect of the keto group is unlikely to be high, at least for the \(\beta\)-keto and the \(\gamma\)-keto esters, we need only to consider the (i) inductive and (ii) the resonance or the mesomeric effects in so far as these may affect the reaction rates. In order to eliminate the uncertainties arising from the use of binary reacting media with different dielectric constants the considerations will mainly
be confined to kinetics carried out only in aqueous medium.

C-I. Inductive Polar Effect.

The Taft values for the inductive polar substituent constants, defined by Ingold-Taft equations, are given for groups CH₃ - CO- and CH₃COCH₂- present in ethyl pyruvate and ethyl acetoacetate. The regularity observed in the additivity of σ* values in the aliphatic domain suggests the feasibility of obtaining σ* value of CH₃-COCH₂-CH₂ - group present in levulinic ester. This can be obtained by dividing the σ* value of CH₃-COCH₂ - group by 2.8. The σ* values, so derived or collected from Taft table, are given below:

<table>
<thead>
<tr>
<th>Group</th>
<th>Present in</th>
<th>σ*</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₃-CO</td>
<td>Ethyl Pyruvate</td>
<td>1.65</td>
</tr>
<tr>
<td>CH₃-CO-CH₂</td>
<td>Ethyl Acetoacetate</td>
<td>0.60</td>
</tr>
<tr>
<td>CH₃-COCH₂-CH₂</td>
<td>Ethyl Levulinate</td>
<td>0.214</td>
</tr>
</tbody>
</table>

These polar inductive constants are based on a scale with methyl (CH₃-) group having a σ* value equal to zero. The values indicate that the rate constants of the alkaline hydrolysis of the three ethyl esters will have magnitudes decreasing in the sequence:

CH₃CO COOC₂H₅ > CH₃COCH₂-COOC₂H₅ > CH₃COCH₂CH₂-COOC₂H₅
The relative values if necessary can be computed from the Taft (loc.cit) relation.

\[
\frac{\sigma_{\text{1}}^*}{\sigma_{\text{2}}^*} = \log \frac{k_1}{k_2}
\]

A look at tables (2B_1 and 2C_1, Chapter 2, pages 66 and 94) shows that this prediction breaks down for the pair ethyl acetoacetate and ethyl levulinate. The alkaline hydrolysis of pyruvic ester belongs to the 'very fast' reaction category and is over in less than a minute or so. Its rate, measured by J. Barthel and G. Bäder\textsuperscript{17} is 48000 \text{lit/mole.min at } 25^\circ \text{C}. This is too high a value to be completely interpreted by a polar factor 1.65 alone. For the \(\beta\) and \(\gamma\) keto esters, the relative rate constant values are just the contrary to what one would expect from the \(\sigma^*\) values. It is, therefore, to be inferred that in all the cases there are factors, besides the polar inductive one, which can even derange the order of the \(\beta\) and the \(\gamma\) keto esters. The factors are the steric and the resonance contributions towards the rate constant magnitudes. The steric influences over alkaline hydrolysis of \(\beta\) and \(\gamma\) keto esters of the present investigations differ very little. The resonance effect, though also similar, leads to a primary \(\pi\) -charge distribution which is strongly
influenced by the proximity or the remoteness of the keto group from the carboxylate unit. It is this factor which perhaps tilts the balance in favour of levulinic ester. This aspect of $\pi$-conjugation and its bearing on reaction rate in the present cases is dealt with in the next section.

The steric and resonance influences in pyruvic ester are widely different from the $\beta$-keto and $\gamma$-keto esters. The resonance phenomenon is treated semiquantitatively to pinpoint this difference.

C-II. $\pi$-Conjugation Effect (Mesomeric Effect) and Relative Rate Constants

Relevant description of calculating the effect of $\pi$-conjugation by H.M.O. technique with parametric modification for heteroatoms has already been presented in the introduction (Chapter 1, page 29). Taking into account the local symmetry of the carboxylate unit, the latter can be regarded as belonging to $C_{2v}$ point group for $\pi$-bonding purposes. Such $\pi$-charge distributions, delocalisation energies and other $\pi$-properties have been found out for the carboxylate unit $\begin{array}{c} 2c \hline \hline 0 \end{array}$ from solutions of the corresponding secular determinant$^{18}$. The results are quoted here
In ethyl acetoacetate the $\beta$-keto group is insulated from the carboxylate unit by a single CH$_2$- group and the $\gamma$-keto group of ethyl levulinate is two such CH$_2$- bonds away. This insulation prevents their participation in the $\pi$-conjugation of the carboxylate unit. So whatever different mesomeric effect the $\beta$-keto and the $\gamma$-keto groups exert on the rate phenomena, this should be a secondary effect viz- a perturbation of the $\pi$-charge on the carboxylate carbon (atom 2) caused by the $\pi$-charge of the $\beta$-carbon and the $\gamma$-carbon of the localised $\pi$-bonding of the carbonyl groups.

It should be noted from the foregoing table that atoms with less than unit electron density (e.g. atom 2) have an essentially positive charge density. Similarly the carbon atom of the $\beta$-keto group of ethyl acetoacetate bears a positive charge density. This latter charge
will, by induction, endeavour to lessen the positive \( X \)-charge density at carboxylate carbon (atom 2). Thus there will be mutual atom-atom polarisation\(^{21} \) between these two atoms. The carboxylate carbon which is the target of nucleophilic attack by \(-\text{OH}\) group in the alkaline hydrolysis mechanism will thus become comparatively less liable for nucleophilic incursion. The rate constant of the alkaline hydrolysis of ethyl acetoacetate will, therefore, be low in spite of the presence of the keto group in the chain and the value will compare favourably with the corresponding non-carbonylated ester viz., ethyl butyrate.

The secondary perturbative influence caused by the \( \gamma \)-keto group on the hydrolytic rate will be practically very little since the \( \text{CO}\)-group is situated far away from the carboxylate unit. It is, therefore, to be expected that the rate constant of the alkaline hydrolysis of ethyl levulinate would be greater than that of ethyl acetoacetate notwithstanding the greater \( \gamma^* \) value of the latter (Sec. C-I, p 127). What is even more, the \( k \)-value for ethyl levulinate is likely to be more than the values observed for noncarbonylated saturated aliphatic acid esters (except Formic acid).
Comparative table for basic hydrolysis of ethyl esters

<table>
<thead>
<tr>
<th>Nature of the ester</th>
<th>Name of the ester</th>
<th>Rate constant lit/mole/min.</th>
<th>Temperature 25°C</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non carboxylated</td>
<td>Ethyl Acetate</td>
<td>6.66</td>
<td>Eero Tommila and Sirkku Hietala</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ethyl Butyrate</td>
<td>2.29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-carboxylated</td>
<td>Ethyl Acetoacetate</td>
<td>3.2</td>
<td>Vide table 2B₁</td>
<td></td>
</tr>
<tr>
<td>γ-carboxylated</td>
<td>Ethyl Levulininate</td>
<td>8.5</td>
<td>Vide table 2C₁</td>
<td></td>
</tr>
</tbody>
</table>

As to the effect of structure on the alkaline hydrolysis of ethyl pyruvate, which is incidentally an extremely fast reaction, the role of C* has already been considered. The mesomeric role can be assessed from the quantitative values of the \( \kappa \)-properties of the structure.

\[
\begin{align*}
\text{CH}_3 & \quad \text{C} \quad \text{C} \\
\text{3} & \quad \text{2} \quad \text{Et} \\
\text{5} & \quad \text{4} \\
\end{align*}
\]

These values are easily calculated by Hückel molecular orbital method with parametric corrections for the coulomb and the resonance integrals.

The nuclear frame-work with the atoms numbered 1 to 5 as shown above has alternating classical double and single
bonds. Calculations show that five \( \pi \)-orbitals are formed, the lowest three of which are filled with six \( \pi \)-electrons contributed jointly by three oxygen and two carbon atoms. The filled orbitals, in order of increasing energy, are

\[
\begin{align*}
\gamma_1 &= 0.834 \phi_1 + 0.435 \phi_2 + 0.216 \phi_3 + 0.239 \phi_4 + 0.118 \phi_5 \\
\gamma_2 &= -0.36 \phi_1 + 0.315 \phi_2 + 0.216 \phi_3 + 0.392 \phi_4 + 0.616 \phi_5 \\
\gamma_3 &= 0.49 \phi_1 - 0.156 \phi_2 + 0.057 \phi_3 - 0.792 \phi_4 + 0.279 \phi_5
\end{align*}
\]

The first two orbitals are bonding and the third is an antibonding one. The \( \pi \)-charge distributions calculated for this \( \alpha \)-keto ester system are shown below.

<table>
<thead>
<tr>
<th>Atoms</th>
<th>( \pi )-charge density in electron charge units</th>
<th>Approximate value of calculated delocalisation energy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-2.131</td>
<td>0.12 ( \beta )</td>
</tr>
<tr>
<td>2</td>
<td>-0.625</td>
<td>( \approx 2 ) to 3 K.Cal/gm mole</td>
</tr>
<tr>
<td>3</td>
<td>-0.586</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>-1.676</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>-0.943</td>
<td></td>
</tr>
</tbody>
</table>

As in the two earlier cases, here the positive charge density at the carbon atom (atom 3) of the \( \alpha \)-keto group will inductively affect the positive charge density at
atom 2, the centre of nucleophilic attack by hydroxyl ion. It is apparent that this effect, though secondary, will be much more pronounced than in the case of $\beta$-keto ester because of the proximity of the $\alpha$-keto group and the carboxylate carbon (atom 2). The natural expectation will be that, so far as the mesomeric effect is concerned, ethyl pyruvate is likely to be less susceptible to alkaline hydrolysis than ethyl acetoacetate or ethyl levulinate. The fact that the contrary is true viz - that it is extremely susceptible to alkaline attack shows that the phenomenon is linked up with the stability problem. The $\pi$-conjugation extending over the nuclear framework is rather fragile since it is not accompanied by efficient lowering of $\pi$-energy — its delocalisation energy, which is a measure of the stability of conjugation, being only 2 to 3 K.Cal/gm mole against the corresponding value of 24 to 26 K.Cal in ethyl acetoacetate or ethyl levulinate. This is not all. One has to consider in addition the hyperconjugation effect of the methyl group to make a fuller treatment of the mesomerism in ethyl pyruvate. And finally the steric influence in the case of ethyl pyruvate is considerably different from what can be expected in ethyl acetoacetate or ethyl levulinate.
Although the discussions of Sections C-I and C-II of the present Chapter have mainly been limited to kinetics in purely aqueous medium, the conclusions reached above can be generally extended to the organo aqueous binary media, as well, having different dielectric constant values.
References

16. ibid, P 592.
References

18. S.C. Rakshit and S. Guha - Private Communication to be Published.

