CHAPTER III.

GENERAL CONCLUSION AND MECHANISM.

SUMMARY.

In this CHAPTER the experimental data reported in the preceding chapter are analysed and certain conclusions drawn. On the basis of this mechanism for the acid catalysed hydrolysis of PFHA is proposed.
The hydrolysis of PFHA has been studied in 1 to 8 molar hydrochloric, perchloric and sulphuric acids. The results show that the reaction is of first order with respect to both the PFHA and the acids, and follow the equation.

\[
\text{Rate} = K [\text{PFHA}] [H_2O]
\]

The results obtained indicate that the reaction is bimolecular. The straight line plots for \(\log K\) against the molar concentration of the acids, i.e. Zucker-Hammett treatment show unit slopes which indicate bimolecular reaction. In perchloric acid the slope is a little below one. In this case the rate of hydrolysis show a linear relation with the concentration of acid between 2 to 7 molar only. The Bunnets' \(^2\) \(\psi\) values 5.4, 4.0, 4.6 and Bunnert and Olsen's \(^3\) \(\phi\) values, 1.04, 1.13 and 1.04, for hydrochloric, sulphuric and perchloric acids respectively, show that the reaction is bimolecular and water acts as a nucleophile and a
proton transfer agent in the rate limiting step. The catalysing action of the acids in the order.

\[ \text{H}_2\text{SO}_4 \succ \text{HCl} \succ \text{HClO}_4 \] further confirms a bimolecular mechanism.

The values obtained for Arrhenius parameters are the energy of activation 22 K cal, frequency factors \(1.58 \times 10^{10}\) litre mole and entropy of activation \(-12E.\) U. The values of the parameters obtained are slightly higher than the values reported for other hydroxamic acids. This indicates that PFHA is more stable in acidic medium as compared to other N-substituted and unsubstituted hydroxamic acids. The negative value of the entropy of activation falls in the range, typical of the reaction proceeding by \(A_2\) mechanism. Reactions following \(A_1\) mechanism show slight positive value of \(\Delta S^+\) and the frequency factor for such reaction is also low.

The formation of 2-furoic acid as one of the products of hydrolysis indicates N-acyl bond fission.
A positive salt effect is observed during the hydrolysis of PFHA in hydrochloric acid in the presence of sodium chloride and in sulphuric acid in the presence of sodium sulphate. Whereas the results of hydrolysis obtained in perchloric acid in the presence of sodium perchlorate show a decrease in the rate of hydrolysis. The studies show that the hydrolysis is an ion-dipolar reaction and the reactive species are the conjugate acid species. These observations point out to a bimolecular mechanism.

In the presence of water-miscible organic solvents decrease in the rate of hydrolysis indicates a more polar character for the transition state. As a result, the complex tends to bind solvent molecules more strongly than do the reactant molecule. This may result to a considerable negative value of entropy of activation and a corresponding low frequency factor. The small value of \( m \), \( m=0.027 \), the sensitivity constant, of Grunwald-Wenstien treatment indicates a bimolecular mechanism. The observations that the hydrolysis is first order with respect to solvent also suggests that the hydrolysis occurs by the \( A^2 \) mechanism.

Distribution of PFHA increases in aqueous phase with the increase in acidity of the solution. In highly acidic medium the protonation of the substrate
takes place to a greater extent rendering it more hydrophilic. The protonation constant (-2.22) determined indicates that it is weakly basic.

The above mentioned conclusions clearly show that the water molecule is involved in the rate determining step and more than one molecule is involved in the transition complex. How many water molecules are actually involved in the formation of the transition complex cannot be ascertained with the present data; because, it is now well recognised that no single acidity function is generally applicable to the protonation behaviour of neutral bases of different structural classes. Yates and his coworkers have analysed the rate data for amide hydrolysis by amide acidity function, $H_A$ and the hydration parameter, $\gamma$, has been calculated using the equation,

$$\log K_{obs} + H_A = \gamma \log a_{H_2O} + \text{constant}. $$

The hydration parameter was found to be approximately three from the hydrolysis data for several amides. This suggests that in the rate determining step one water molecule attacks the conjugate acid as a nucleophile and two more water molecules on the average assist by hydrogen bonding.
In the absence of an acidity function for the hydroxamic acids, the method proposed by Yates and Meelelland is worth trying. They proposed the method for finding a suitable acidity function, $H_s$, for determining the hydration parameter in ester hydrolysis which is a modification of the Bunnett treatment. The general rate scheme for ester hydrolysis in terms of fully hydrated species was written as

$$
S(H_2O)_n + H^+ (H_2O)_p \xrightarrow{\text{fast}} SH^+ (H_2O)_p + (S+n+p)H_2O \xrightarrow{\text{fast}} SH^+ (H_2O)_p + H_2O \xrightarrow{\text{Slow}} S(H_2O)_n \rightarrow \text{Products}
$$

The simple relationship between rate, acidity, and water activity was derived from transition state theory and was represented by the equation.

$$
\log K_1 + H_s = \log a_{H_2O} + \text{constant.}
$$

$K_1$ being the pseudo first order rate constant. The relationship between measured ionization ratios for esters and the acidity function, $H_s$, was shown as

$$
\log \frac{[SH^+]}{[S]} = -H_s + pK_{SH} +
$$

The ionization ratios were measured spectrophotometrically for several acetate esters and a line as
relationship was obtained using $H_0$ data for the equation

$$\log \frac{[SH^+]}{[S]} = -mH_0 + \text{constant}.$$ 

The slope $m$ were found to be approximately 0.62 for acetate esters. Assuming this value to be valid for all esters, they calculated the hydration parameter, $r$, and obtained a value of 2.

Tillet and his coworkers studied the protonation behaviour of some para substituted benzo hydroxamic acids. The values of ionisation ratios determined by him were utilised here for plotting them against the corresponding values of $H_0$. The value of the slope 'm' determined was found to range from 0.58 to 0.68. If the average value of four hydroxamic acids falling in a close range, is taken as 0.60, the new acidity function, $H_s$ is calculated and is shown in Table 1. When $(\log K_1 + H_s)$ is plotted against $\log a_{H_2O}$, a straight line is obtained with a slope of 1.91 as presented in Figure 1. This observation indicates that two water molecules are involved in the formation of the transition complex formed during the acid catalysed hydrolysis of PFHA. The necessary data are given in Table 1.

A reasonable mechanism on the basis of the results obtained for the hydrolysis of PFHA may thus involve the following steps. The PFHA first gets protonated with a rapid establishment of the protonation equilibrium
Water molecule then reacts slowly with the protonated substrate and thus forms a transition complex which may in turn results to the products. Formation of 2-furoic acid and phenyl hydroxylamine during hydrolysis indicates N-acyl bond fission. Earlier workers have also arrived to the similar conclusions.
**TABLE 1.**

<table>
<thead>
<tr>
<th>[HCl] M</th>
<th>H₀</th>
<th>Hₜ</th>
<th>Log K₁*</th>
<th>log K₁+Hₜ</th>
<th>Log qH₂O</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-0.21</td>
<td>-0.126</td>
<td>-1.283</td>
<td>-1.406</td>
<td>-0.017</td>
</tr>
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<td>2</td>
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<td>-0.492</td>
<td>-1.067</td>
<td>-1.472</td>
<td>-0.039</td>
</tr>
<tr>
<td>3</td>
<td>-1.05</td>
<td>-0.620</td>
<td>-0.923</td>
<td>-1.550</td>
<td>-0.070</td>
</tr>
<tr>
<td>4</td>
<td>-1.41</td>
<td>-0.846</td>
<td>-0.815</td>
<td>-1.666</td>
<td>-0.107</td>
</tr>
<tr>
<td>5</td>
<td>-1.76</td>
<td>-1.057</td>
<td>-0.729</td>
<td>-1.786</td>
<td>-0.155</td>
</tr>
<tr>
<td>6</td>
<td>-2.12</td>
<td>-1.372</td>
<td>-0.557</td>
<td>-1.932</td>
<td>-0.211</td>
</tr>
<tr>
<td>7</td>
<td>-2.53</td>
<td>-1.618</td>
<td>-0.595</td>
<td>-2.118</td>
<td>-0.279</td>
</tr>
<tr>
<td>8</td>
<td>-2.93</td>
<td>-1.758</td>
<td>-0.541</td>
<td>-2.398</td>
<td>-0.358</td>
</tr>
</tbody>
</table>

*The values of the rate constant K₁ are for the hydrolysis in HCl at 60.1°C.*
The formation of a tetrahedral addition intermediate in this system can be presumed by analogy to the hydrolysis of other carboxyl derivatives. In fact, Bunnell suggested general acid catalysis of the breakdown of the tetrahedral intermediate as an explanation of the high observed value of ω for ester hydrolysis by AAc mechanism. In the present studies the ω parameters obtained are 5.4, 4.0 and 4.6 for HCl, H₂SO₄ and HClO₄ respectively.

The full mechanism based on these conclusions can be written as:

1. \[ C₆H₅ O H + H₃O^+K_1 \xrightarrow{\text{fast}} C₆H₅OH^+ \]
2. \[ C₆H₅ OH^+ + H₂O \xrightarrow{\text{fast}} C₆H₅ OH \]
3. \[ C₆H₅ OH + H₂O \xrightarrow{\text{slow}} C₆H₅ OH + OH^- \]
4. \[ C₆H₅ OH + H₂O \xrightarrow{K_2 \text{ (fast)}} C₆H₅ OH + H₂O \]
5. \[ C₆H₅ OH + H₂O \xrightarrow{K_3 \text{ (slow)}} C₆H₅ OH + H₂O \]
6. \[ C₆H₅ OH + H₂O \xrightarrow{K_4 \text{ (fast)}} C₆H₅ OH + H₂O \]
7. \[ C₆H₅ OH + H₂O \xrightarrow{K_5 \text{ (slow)}} C₆H₅ OH + H₂O \]
8. \[ C₆H₅ OH + H₂O \xrightarrow{K_6 \text{ (fast)}} C₆H₅ OH + H₂O \]
9. \[ C₆H₅ OH + H₂O \xrightarrow{K_7 \text{ (slow)}} C₆H₅ OH + H₂O \]
10. \[ C₆H₅ OH + H₂O \xrightarrow{K_8 \text{ (slow)}} C₆H₅ OH + H₂O \]
The rate expression for the disappearance of the hydraxamic acids, S can be given, as in the case of ester hydrolysis by the use of the steady state approximation for the tetrahedral intermediate, by the equation.

\[
\frac{-d[S]}{dt} = \frac{K_3 K_5 \cdot [SH^+] \cdot [H_2O]^2}{K_4 + K_5}
\]  

(1)

Considering the equilibria for the two reactions

1. \( H_2O^+ \rightleftharpoons H^+ + H_2O \)

\[
K_W' = \frac{[H^+] \cdot [H_2O]}{[H_3O^+]} \]

or \( [H^+] = \frac{K_W' \cdot [H_3O^+]}{[H_2O]} \)  

(2)

2. \( SH^+ \rightleftharpoons S + H^+ \)

\[
K_a = \frac{[S] \cdot [H^+]}{[SH^+]} \]

or \( [SH^+] = \frac{[S] \cdot [H^+]}{K_a} \)  

(3)

Substituting \([H^+]\) from equation 2, equation 3, can be written as

\[
[SH^+] = \frac{[S] \cdot [H_3O^+] \cdot K_W'}{K_a \cdot [H_2O]} 
\]

(4)
Substituting this value of $[\text{SH}^+]$ in equation 1,

$$\frac{-d[S]}{dt} = \frac{K_3K_5K'_w[S][\text{H}_3\text{O}^+][\text{H}_2\text{O}]}{K_a(K_4 + K_5)}$$

where $K'_w$ is the dissociation constant of the hydronium ion and $K_a$ is the dissociation constant of the protonated hydroxamic acid.

The formation of a symmetrical tetrahedral addition can be determined by $^{18}$O trace technique. For want of facilities this experiment could not be conducted. However, the high value of Bunnett's $W$ parameter and the involvement of water as a proton transfer agent are indicative, though not conclusive, for such an inference.
REFERENCES.

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