

### 6.2.2.5. Specific and General Acid-Base Catalysis

A catalyst is a substance which increases or decreases the reaction rate without itself being altered chemically. A catalyst does not alter the equilibrium of a reversible reaction but speeds up the reaction so that the equilibrium is attained in a shorter time. A catalyst acts by combining with the reactant to form an activated intermediate complex which decomposes to give the catalyst and the product. Most of the chemical reactions are catalysed by catalysis.

There are generally two types of catalysts, which are:

- 1) **Specific Acid-Base Catalysis:** A number of drugs in solution undergo hydrolytic degradation in solution upon addition of an acid or a base. If the drug solution is buffered, the decomposition may not be accompanied by a significant change in the concentration of acid or base, so that the reaction may be considered to be catalysed by hydrogen or hydroxyl ion. When the rate equation for such a reaction is found to contain a term involving the concentration of hydrogen or hydroxyl ion, the reaction is said to be specific acid-base catalysed.

The effect of hydrogen or hydroxyl ion concentration on specific acid or base catalysed reactions can be expressed in the form of the following rate equation:

$$dP/dt = (k_0 + k_1[H^+] + k_2[OH^-]) [S]$$

For which the observed rate constant is given by:

$$k_{\text{obs}} = k_0 + k_1[\text{H}^+] + k_2[\text{OH}^-]$$

At low pH, the hydrogen ion concentration is high and hence  $k_1[\text{H}^+]$  is greater than  $k_0$  or  $k_2[\text{OH}^-]$ . The observed reaction rate constant becomes:

$$k_{\text{obs}} = k_1[\text{H}^+]$$

And the reaction is specific hydrogen ion catalysed or acid catalysed.

Similarly, at higher pH, the hydroxyl ion concentration is much higher and hence the term  $k_2[\text{OH}^-]$  be greater than  $k_0$  or  $k_1[\text{H}^+]$ . The observed reaction rate becomes:

$$k_{\text{obs}} = k_2[\text{OH}^-]$$

And the reaction is specific hydroxyl ion or base catalysed. At an intermediate pH, when the concentrations of hydrogen and hydroxyl ions are low or if the products of  $k_1[\text{H}^+]$  and  $k_2[\text{OH}^-]$  are small in value, the observed reaction rate is:

$$k_{\text{obs}} = k_0$$

In this case, the reaction is said to be solvent catalysed.

If the pH of the reaction medium is slightly acidic, both solvent and specific acid catalysis are involved. In case the reaction medium is slightly alkaline, both solvent and specific base catalysis are involved in the degradation process.

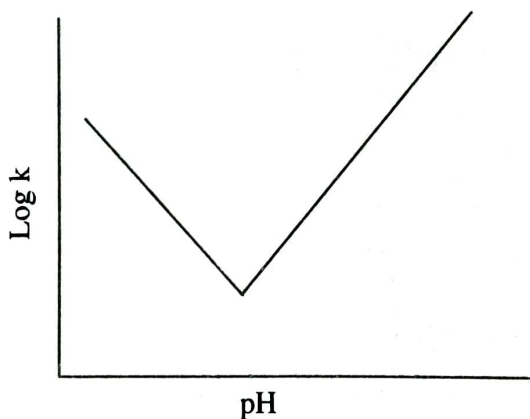


Figure 6.3: pH Rate Profile

The effect of pH on the degradation may be determined by obtaining the pH-rate profile for the specific acid-base catalysed reaction. In this, the degradation at several hydrogen ion concentrations (pH) is determined and a plot is obtained by plotting the log of rate constant ( $\log k$ ) against pH (figure 6.3). The point of inflection of such a plot gives the pH of maximum stability.

- 2) **General Acid-Base Catalysis:** The acid-base catalysis in solutions is not restricted to hydrogen or hydroxyl ions only, but often undissociated acids or bases also produce a catalytic effect on the reaction. Such reactions are said to be general acid and base catalysed reactions. **For example**, most of the pharmaceutical formulations employ buffers for maintaining the pH or the



solution. Often, one or more components of the buffer catalyse the rate of reaction. If the catalytic component is acidic, the reaction is said to be subjected to general acid catalysed and if the component is basic, the reaction is said to be general base catalysed. Common buffer salts that have a catalytic effect are acetate, phosphate and borate buffers.

In order to determine whether a reaction is being catalysed due to the presence of a buffer system, different solutions are prepared at the same pH (by keeping the ratio of the buffer components constant) but at different concentration of the buffer components. The rate of degradation is determined and if it is found to vary with the concentration of the buffer components, the reaction is said to be general acid-base catalysis.