Unit - V

Influence of temperature on rate of rxn

* The speed of many rxn rises about two or 3 times with every 10 degree rise in temperature.

* Arrhenius equation explain the effect of temperature.——

$$K = Ae^{-Ea/RT}$$

Integration of eqⁿ——

$$\ln k = \ln A - \frac{Ea}{RT} \ln e$$

log form of equation

$$\log k = \log A - \frac{Ea}{2.303 \, RT}$$

k = specific rate constant.   R = Ideal gas constant

A = Frequency factor   T = Absolute temp.

Ea = Energy of activation

* Energy of activation is defined as minimum energy that a molecule possess to induce molecules collision to form product.

* Arrhenius factor (A) is defined as the frequency of collision b/w molecules.

* Collision theory states that collision must occur b/w molecules.

* The r×n b/w molecules does not take place unless they have certain energy.

* At any given temperature, a fix number of molecules have certain energy.

* As the temperature rises more of molecules absorb energy and get activated.

* These activated molecules are responsible for ↑ed rate of r×n.

Influence of solvent on rate of cr^n

* The effect of solvent is related to the relative solubility of the reactants and the product in the given solvent.

$$A + B \longrightarrow (A - - + B) \longrightarrow product.$$
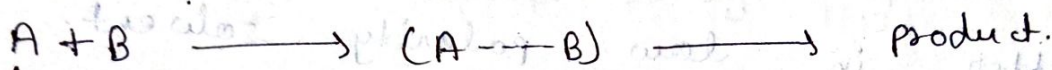
* The equantitative relationship b/w cr^n rate constant and the solubility is given by equation —

$$\log k = \log k_0 + \frac{V}{2.303R} \cdot \frac{1}{T} (\Delta \delta_A + \Delta \delta_B - \Delta \delta^*)$$

$k =$ cr^n rate constant

$k_0 =$ Rate constant in infinitely dilute soln.

$V =$ Molar volume of reactants (A and B)

$\delta_A, \delta_B, \delta^* =$ solubility parameter of reactants A, B and complex.

* Polar solvent tend to accelerate rxn in which the product formed are more polar than the reactants.

* If the product formed are less polar then the reactant, then the rxn proceed better in low polarity solvent.

* Examples of non-aqueous solvent —

ethanol, Glyceral, propylene glycol, vegetable oil etc.

Influence of ionic strength on rate of rxn

* The effect of ionic strength of a salt on rate of rxn may be expressed by following equation —

$$\log k = \log k_0 + 1.02 \, Z_A Z_B \sqrt{\mu}$$

Where → k = degradation rate constant for the rxn

k₀ = Rxn rate constant at infinite dilution.

Z_A and Z_B = charges carried by the reactants A and B.

$\sqrt{\mu}$ = Ionic strength of the salⁿ.

* A/c to above equatⁿ, ____ Increase in ionic strength ↓es the rate of rxn involving interaction b/w oppositely charged ions.

* It ↑es the rate of rxn b/w similarly charged ions.

* Rxn's which result in formatⁿ of oppositely charged ions (Product). Exhibit ↑ in rxn rate an ↑ing ionic strength.

Ex-1 $A^+ + B^-$ ⟶ C + D (↓)

        $A^+ + B^+$ ⟶ C + D (↑)

        A + B ⟶ $A^- + B^+$ (↑)
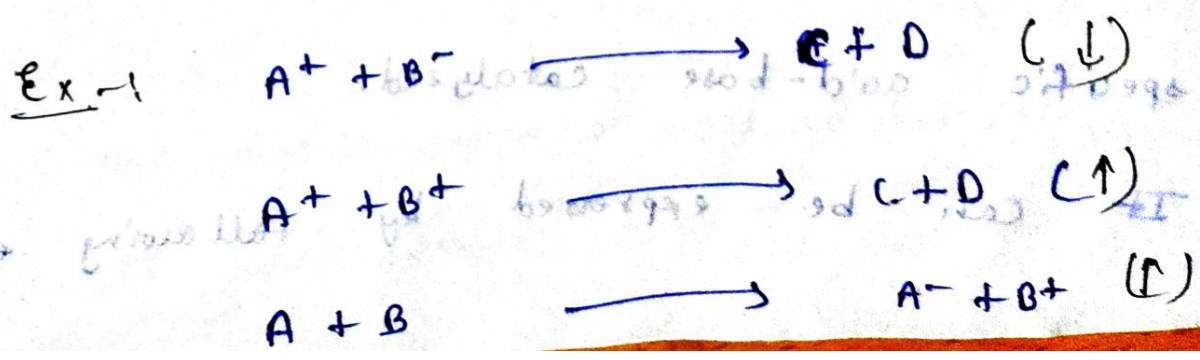
Specific and general acid - base catalysis

Ionic form   Unionform

Catalyst :-

A catalyst is defined as a substance which ↑es or decreases the rate of rxn without itself being changed chemically.

* A catalyst doesnot alter the equilibrium of reversible rxn.

* There are fallowing types of catalysis —

1- Specific acid -base catalysis :-

If dry salt is buffer, ~~they~~ decomposition may nat takes place by change in concentrath of acid ar base.

* The rxn may be catalysed by H^+ ar OH^-.

* When the rate equath involving concentrath of H^+ ar OH^-, the rxn is said to be specific acid-base catalysed.

* It can be expressed by fallowing equath

$$\frac{d\rho}{dt} = (k_0 + k_1 [H+] + k_2 [OH^-]) [S]$$

* Observed rate constant is given by —

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

* At low pH, the H^+ ion concentration is greater than k_0 and $k_2 [OH^-]$.

The observed rate constant becomes —

$$k_{obs} = k_1 [H+]$$

The rxn is acid catalysed.

* At higher pH, the OH^- concentration is greater than k_0 + $k_1 [H^+]$.

The observe rxn rate becomes —

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

The rxn is based catalysed.

* At intermediat pH, the concentrath of H^+ and OH^- are low.

The observed rxn rate is →

$$K_{obs} = k_o$$

The rxn is said to be solvent catalysed.

2 - General acid - base catalysis -:

A rxn in which undissociated acid or base produce catalytic effect on the rxn are

K/as general acid - base catalyst.

Ex → P'ceutical formulation used buffers for maintaining the pH of the soln.

→ One or more components of the buffer catalyse the rate of rxn.

→ If the catalytic component is acidic, the rxn is said to be general acid catalysed.

→ If the catalytic component is basic, the rxn is said to be general base catalysed.

Influence of dielectric constant on rate of reaction

* The dielectric constant (kddy) of the solvent has effect on rate of rxn.

* It is given by equation —

$$\ln k = \ln k_{\varepsilon = \infty} - \frac{N Z_A Z_B \, e^2}{R T \, r^*} \cdot \frac{1}{\varepsilon}$$

$$\int k = \int k_{\varepsilon = \infty} - \frac{N Z_A \cdot Z_B \, e^2}{R T \, r^*} \cdot \frac{1}{\varepsilon}$$

where ;

$k =$ observed rxn rate in a solvent.

$k_{\varepsilon = \infty} =$ Rxn rate constant of a solvent of infinite dielectric constant.

$N =$ Avogadros number.

Z_A and $Z_B =$ charges on ionic species.

$e =$ Unit of electric charge.

$r^* =$ Distance b/w ionic species

$\varepsilon =$ Dielectric constant of the sol".

* Rxn involving ions of opposite charge are accelerated by ~~solvent~~ law dielectric constant.

* In rxn's having similarly charged species the rate of rxn is ↑ed by high dielectric constant solvent.

* Rxn b/w neutral molecules enhence/↑ed by high dielectric constant

Rate of rxn

* The rate is defined as the velocity with which a reactant or reactants undergo chemical change.

* It can therefore be measured by measuring the change in the concentration of a reactant or product in a particular period of time.

* It is given by $\pm \dfrac{dc}{dt}$,

Rate constant :

According to law of mass action, the rate of a chemical rxn is proportional to the product of molar concentration of reactants raised to a power equal to the number of molecules a and b of the substance A and B.

$$aA + bB \longrightarrow C$$
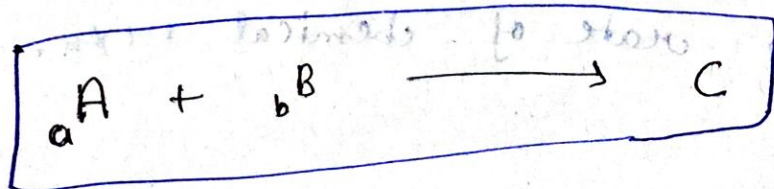
Rate of rxn is given by ____

$$\text{rate} = \frac{-1}{a} \frac{dA}{dt}$$

$$\text{Rate} = \frac{-1}{b} \frac{dB}{dt}$$

$$\text{Rate} = k [A]^a [B]^b$$

In this small k is rate constant.

Order of reaction →

The order of rxn is the sum of the power of the concentration involved in the rate equation.

* The order of above rxn is (a+b).

* The order of rxn refers to the way in which the concentration of reactent or reactants influence the rate of chemical rxn.

1- Zero order orth :-

       If the rate of a orth is independent of the concentration of reacting species, the orth is said to be zero order orth.

     The rate of zero order orth is given by —

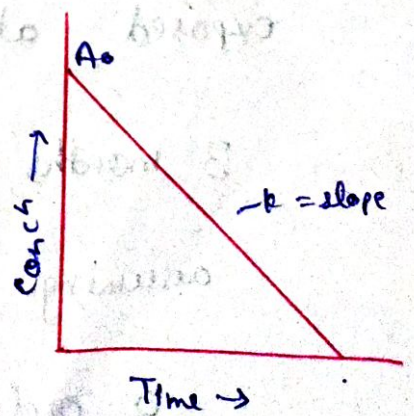$$A \longrightarrow \boxed{Product}$$
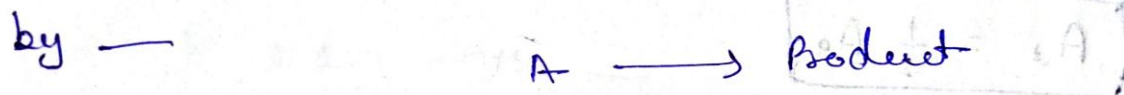
$$\boxed{\dfrac{-dA}{dt} = k}$$

* dA is the change in concentration with respect to change in time.

* (−) indicates the concentration after time interval (t).

$$\int_0^t dA = -k \int_0^t dt$$

$$A_t - A_0 = -kt$$

$$\boxed{A_t = A_0 - kt}$$

0 (zero) order half life

Half life ($t_{1/2}$) of a chemical with is the time required for the initial concentration of the reactant to get reduced to half.

$$\boxed{A_t = \frac{1}{2} A_0}$$

Substituting —

$$A_t = A_0 - kt$$

$$\frac{1}{2} A_0 = A_0 - kt_{1/2}$$

$$\boxed{kt_{1/2} = \frac{A_0}{2}}$$

$$\boxed{t_{1/2} = \frac{1}{2} \frac{A_0}{k}}$$

Q-1→ The colour intensity of a drug preparation exposed at 45°c led from 1.420 — 1.400 in 3 months. stimate the reaction rate. assuming that the colour feding follows 0 order with.
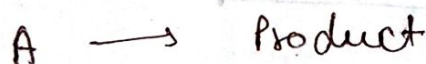
Ans→1

$$1.400 = 1.420 - k \times 90$$

$$90k = 0.020$$

$$\boxed{k = 0.0002}$$

2— **First order rxn** →

When the rate of rxn is directly proportional to the first power of the concentration of a single reactant, the rxn is said to be first order rxn.

$$A \longrightarrow Product$$

The rate of rxn is first order.

$$-\frac{dc}{dt} = kC$$

$$\frac{dc}{C} = -kdt$$

Integration of equation____

$$\int_0^t \frac{dc}{C} = -k \int_0^t dt$$

$$\ln C - \ln C_0 = -kt$$

$$\boxed{\ln C = \ln C_0 - kt}$$

log form —

$$\log C = \log C_0 - kt/2.303$$

$$\boxed{K = \frac{2.303}{t} \log \frac{C_0}{C}}$$

Exponential form —

$$\boxed{C = C_0 e^{-kt}}$$

First order half life

Definition same as 0 order —

$$t_{1/2} = \frac{C_0}{1/2}$$

$$t = \frac{2.303}{K} \log \frac{C_0}{C}$$

$$t = \frac{2.303}{K} \log \frac{C_0}{\frac{1}{2}C_0}$$

$$\boxed{t_{1/2} = \frac{0.693}{k}}$$

Q-1 → A salt of drug cantain 680 units/ml when prepared. It was analysed after a period of 60 days and was found to contain 400 units/ml. Assuming that they composition is first order, at what time will the drug have decomposed to ½ of its original concentration.

Ans →

$$60 = \frac{280}{k}$$

$$k = 4.66$$

$$\text{longitdy}_{1/2} = 0.17$$

because concentration

Isobal t/c -0.8

3- Second order rth -:

A reaction is said to be second order, when the overall order is two.

* The rate of second order rxn may be proportional to the product of two concentratio

* Example are —

$$NO_2 + CO \longrightarrow NO + CO_2$$

→ This is second order in the reactant NO_2 and zero order in the reactant CO.

→ The observed rate is independed of concentra of CO.

→ The rate of rxn is proportional to concentration squared.

Photolytic D.-:

Decomposition of drug substance by light is called as photo degradation. light energy catalyzed or initiate some rxn.
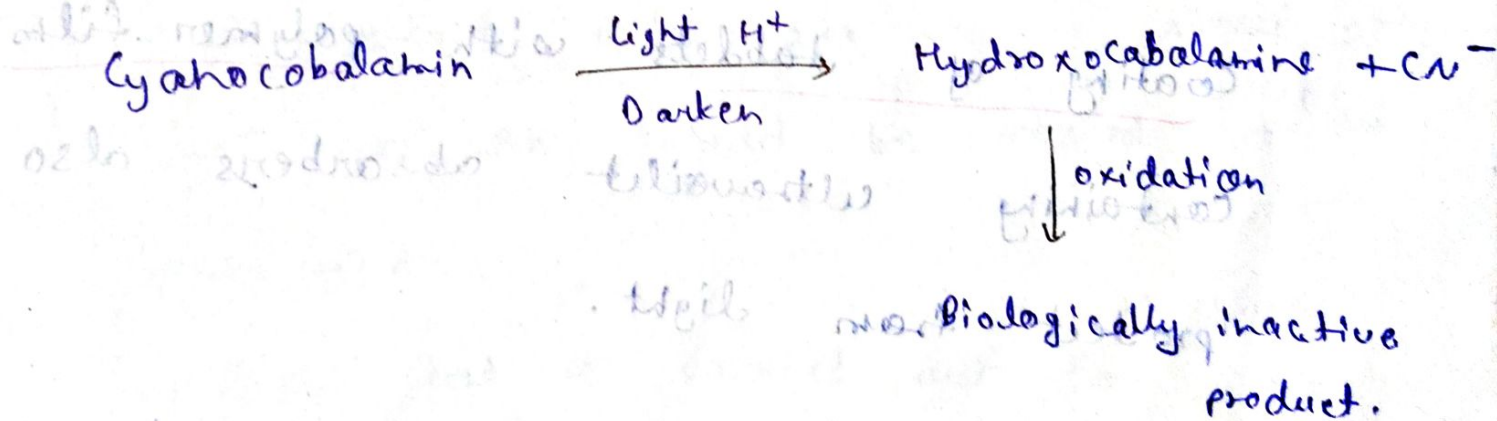
Photolytic degradation

* Many p'ceuticals compounds including ascorbic acid, cyanocobalamines, riboflavin, folic acid, hydro cortisole, prednisonal etc. undergo degradation when it exposure to light.

* Exposure to light may produce oxidation and reduction, using arrangement, molification and polymerization.

Ex-1

$$Cyanocobalamin \xrightarrow[Darken]{Light, H^+} Hydroxocabalamine + CN^-$$

with oxidation arrow pointing down to:

Biologically inactive product.

* Photochemical may be accompanied by thermal rxn.

* The thermal rxn ance induced by light may continue after the light source has been

withdrawn.

* prevention :-

It can be reduced by using amber coloured glass container.

— By using black thermo setting plastic it can also be reduced.

— By storing product in dark place on by packing in cartons also act as varrier to light.

— Coating of tablets with polymer film containing ultraviolet absorbers also protect from light.

— Ordinary containers can be wrapped with black paper also. provide protection agai light.

Accelerated stability testing in expiration dating

1- Accelerated stability testing-;

Stability is defined as the time during which the drug product regions the same properties existing at the time of manufacture.

* Accelerated stability test is designed to test stability and set self life of formulations under narmal or recommeded storage condition.

* The study is carried out under accelerated condition of temp. moisture and light.

* The product which are to be stored 25°c and 45% Rh should be stored at 40°c and 60% Rh.

* Similarly test is carried out for product to be stored cool and cold temperature.

Common high stress conditions are—

① Temperature →

↑es in temperature increase.

degradat^n.

Ⅱ Humidity →

High humidity results in hydrolysis.

Ⅲ Light →

Artificial light can be used to accelerate the effect of sun light.

2- Self life →

It is defined as the time required for the conc. of the reactant to reduce 90% of it's original/initial conc.

* The various steps for self life are as follows—

→ Each partion is stored at different temp. such as 40°C, 50°C, 60°C, 70°C.

→ Samples from each partion are withdrawn at various interval of time.

→ The order of reaction is determine by plotting conc. verses time graph.

→ The slop of line gives the rate constant 'k' for degredation at each temperature.
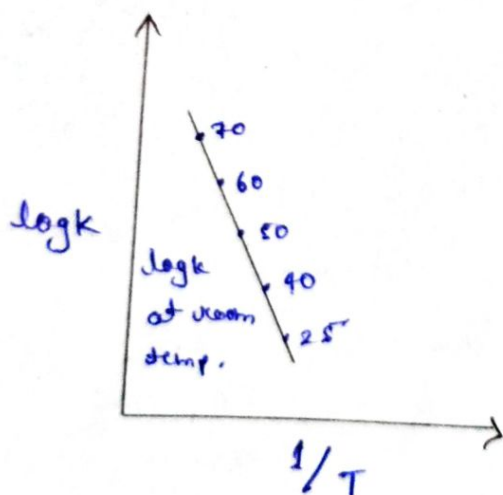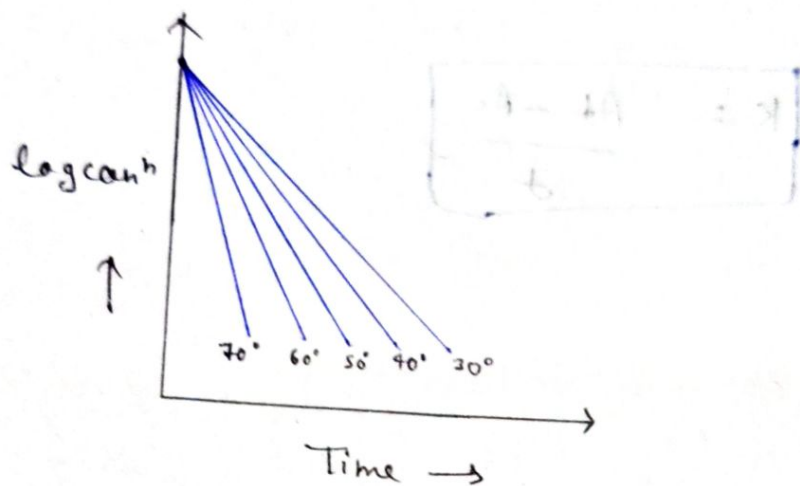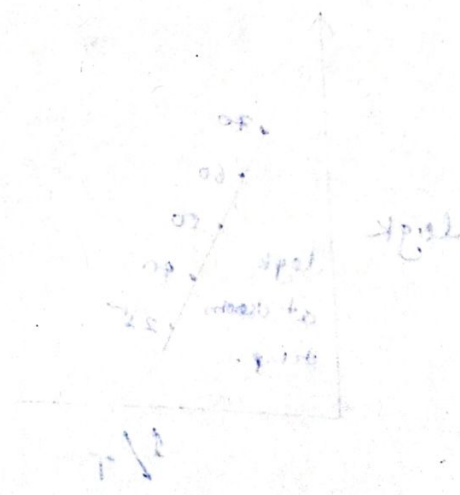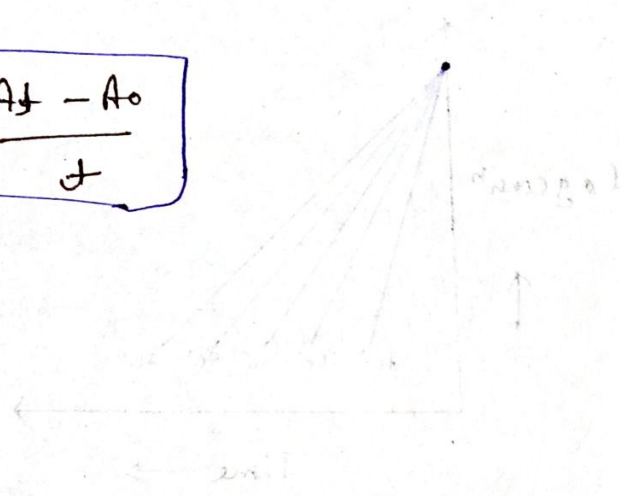

→ From arrhenious equations, the rate constant 'k' for degradation at room temp (25°c) is determined.

$$k = Ae^{-Ea/RT}$$

* The value of 'k' at 25°C is substituted in appropriate rate equation and estimate for self life of the product is obtained.

$$k = \frac{2.303}{t} \log \left(\frac{C_0}{C}\right)^{1/t}$$

$$\boxed{k = \frac{At - A_0}{t}}$$