

PHARMACEUTICS 3

سوتكس ٣

chapter : Kinetics part 2

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Second-Order Reaction

1) $A+B \rightarrow \text{products}$

باول نوع عنا مادتين
مختلفتين يتفاعلو مع بعض

$$-d[A]/dt = -d[B]/dt = k[A][B]$$

- let x be the concentration of each species reacting in time, then the rate of reaction, $dx/dt = k(a-x)(b-x)$
- When both A and B are present at the same concentration so that $a=b$ then $dx/dt = k(a-x)^2$

$$dx/(a-x)^2 = k dt$$

- Integration using the condition $x=0$ at $t=0$ and $x=x$ at $t=t$

$$\int_0^x \frac{dx}{(a-x)^2} = k \int_0^t dt$$

$$\left(\frac{1}{a-x} \right) - \left(\frac{1}{a-0} \right) = kt$$

نوت عجنب: بس نشوف $A-x$ او $B-x$ هاد
معناه انو تركيز B و A قاعد بقل بمرور
الوقت بمقدار x ويلى هو اشي منطقي لانه
المواد عم تتفاعل فرح تنقص ☺

$$\frac{x}{a(a-x)} = kt$$

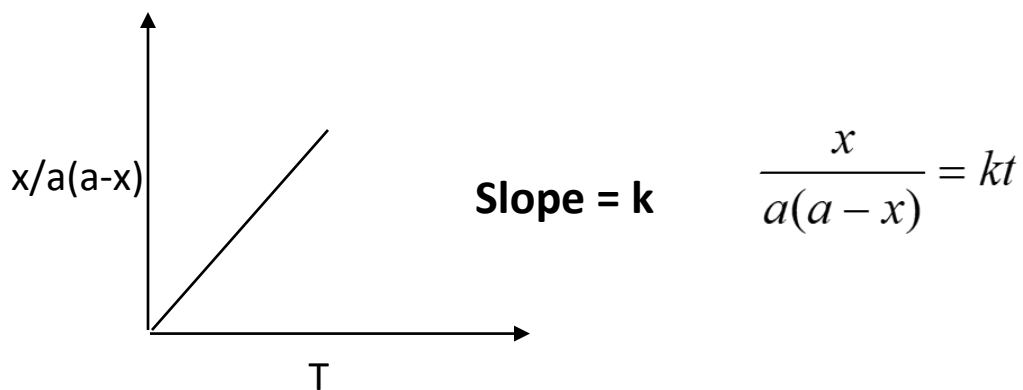
$$\frac{1}{at} \frac{x}{(a-x)} = k$$

هدول الاشتقاقات مو مهمة

بس هاد القانون نركز عليه ويلى بمثل ال

Second order reaction equation for the first type





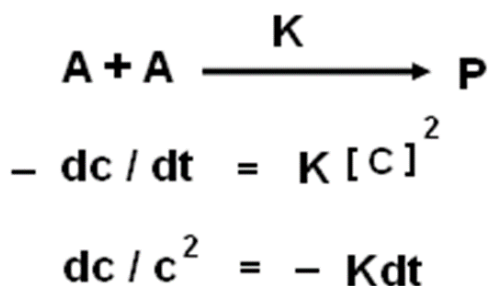
- When, $x/a(a-x)$ is plotted against t a **straight line** results if the reaction is **second order**.
- The slope of the line is k .
- **Half-Life** of a second order reaction:

$$t_{1/2} = 1/ak$$

- **Shelf life:**

$$t_{0.9} = 0.1/(0.9 \cdot a \cdot k)$$

2) When you have one component reacting with itself



هون عنا نفس المادة بتتفاعل مع
حالتها

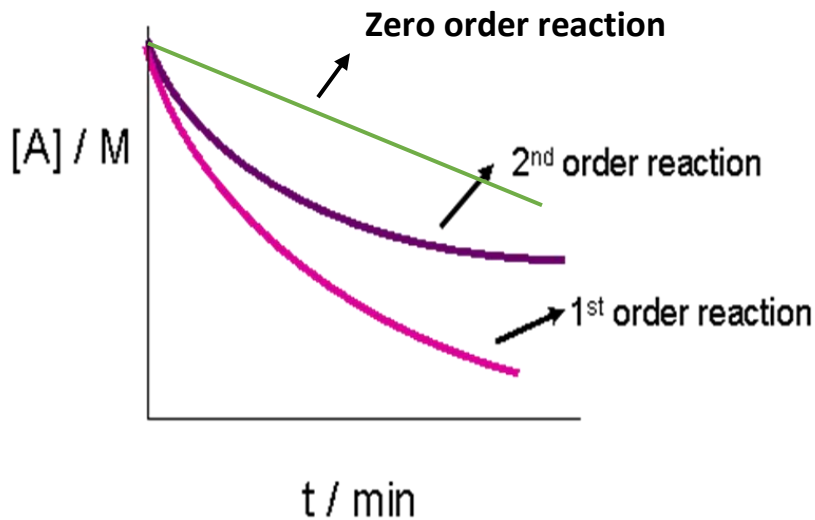
Equation:

$$1/C = 1/C_0 + Kt$$



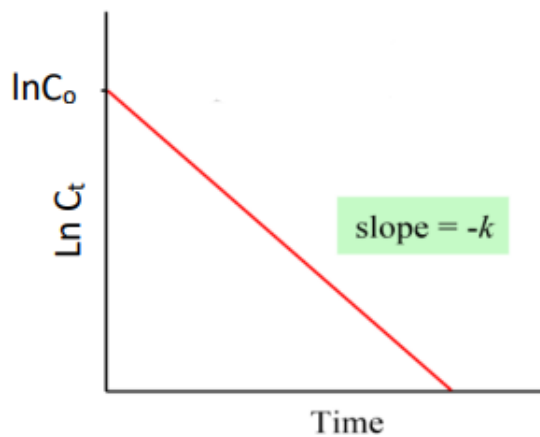
Second order equation for
the second type

- ممكن يجينا تلت انواع رسومات ولازم نحدد منهم ال order of the reaction :



1- y-axis = concentration
and x-axis = time
And the line is linear
The reaction is **zero order**

If Same axis but not linear, it could be **first order or second order**



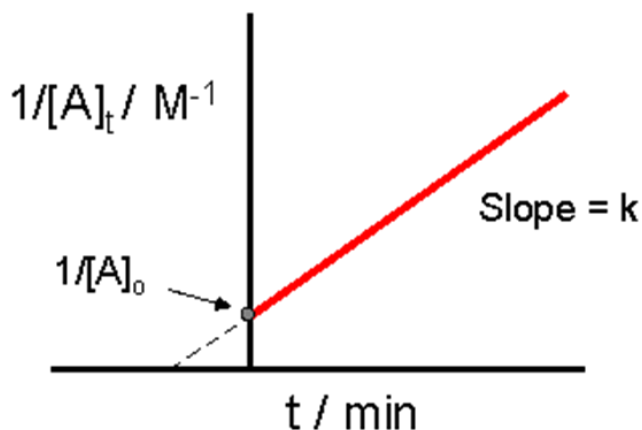
2- y-axis = $\ln C_t$

X-axis = time

And the line is linear, the reaction is **first order**

If not linear, it is **second order**

**هاي الرسمة كانت بالبارت الماضي اتذكروها



3- y-axis = $1 / \text{concentration}$

x-axis = time

and the line is linear, it is **Second order reaction**

Classic Collision Theory of Reaction Rates

- Consider a situation in which all the molecules of a substance are moving in the same direction at the same velocity. If a molecule **deviates** from its course, it will collide with another molecule, causing both molecules to move off different directions with different velocities. A **chain of collisions** between different molecules can then occur, which finally results in random motion of all molecules. In this case, only a certain fraction of the molecules has a velocity equivalent to the initial velocity of the ordered system.

افتراضو انو كان في عنا جزيئات بتحركو بنفس الاتجاه بسرعة متساوية وواحد منهم حاد عن مساره، حياده رح يؤدي لاصطدامه مع جزيئ اخر ويصيرو التنتين يتحركو باتجاه مختلف وسرعة مختلفة، وحيصير سلسلة تصادمات بعدها وبالاخير جزيئات قليلة يلي حيزلو محافظين على نفس السرعة الاولية ونفس الاتجاه

- The net result a distribution of molecular velocities varying from zero upward is attained and this corresponds to the distribution of molecular energies (kinetic energy is proportional to the square root of velocity)
وبعدين كل جزيئ حيزير عنده طاقة حركية مختلفة وهاي الطاقة علاقتها طردية مع الجذر التربيعي للسرعة
- The theory postulates that a collision must occur between molecules for a reaction to occur and, further, that the reaction between molecules does not take place unless the molecules **are of a certain energy.**
ومشان يصير التفاعل بين الجزيئات المتصادمة لازم يمتلكو طاقة حركية كافية لحدوث التفاعل
- The rate of the reaction can be considered proportional to the number of moles of reactant having sufficient energy to react.

$$(1) \quad f_i = N_i/N_T = e^{-E_i/RT}$$

Where N_T is the total number of moles, N_i is the number of moles having a kinetic energy of E_i and f_i is the fraction of molecules having sufficient energy, E_i , for reaction.

$$(2) \quad \text{Rate} = PZ N_i$$

Where **Z**: number of collisions per second per cm³ or collision frequency(constant),
p: probability factor, which gives the probability that a collision between molecules will lead to a product (constant).

$$\text{Rate} = (PZ e^{-E_i/RT}) N_T \longrightarrow$$

عوضنا اول معادلة في ثاني معادلة
 ولانه يلي داخل القوس كله ثوابت حنعتبر عنه ب K

Since Rate = k x Concentration

$$k = PZ e^{-E_i/RT}$$

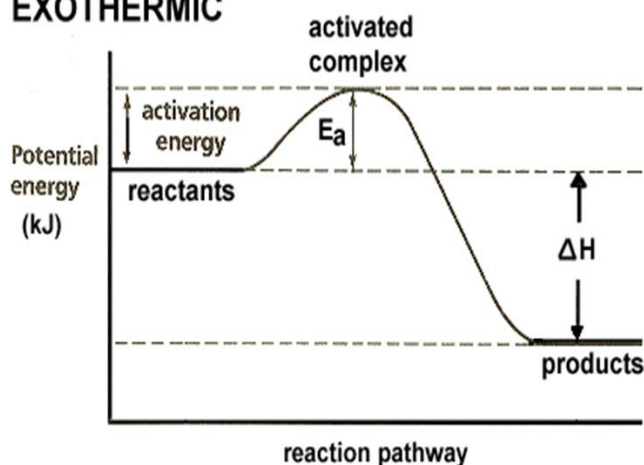
$$A = PZ$$

$$E_a = E_i$$

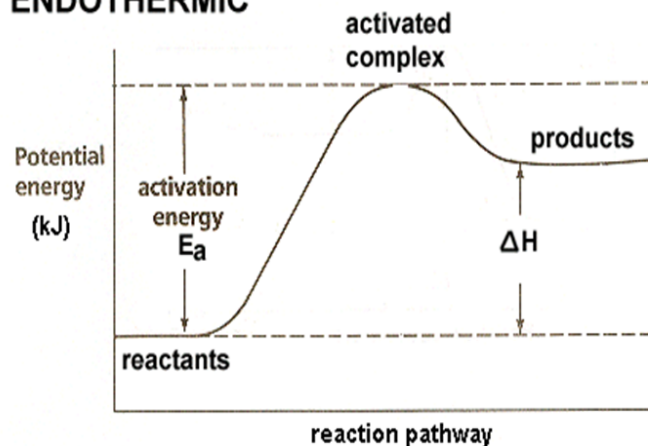
$$k = A e^{-E_a / RT}$$

معادلتننا بتربط بين درجة الحرارة وتأثيرها
 على سرعة التفاعل (Rate of reaction)

EXOTHERMIC



ENDOTHERMIC



عنا نوعين من التفاعلات:

1. الماص للحرارة: يحتاج طاقة مشان يكون نواتج ويصير التفاعل وكل ما زادت درجة الحرارة بتزيد سرعة التفاعل
2. الطارد للحرارة: بس يصير التفاعل بحرر طاقة وبس تزيد الحرارة بتقل سرعة التفاعل

TEMPERATURE EFFECTS

- Reaction rates are expected to be **proportional** to the number of collisions per unit time which increases with increasing temperature.
- The speed of many reactions increases 2 to 3 times with each 10° rise in temperature.
- As a reaction proceeds, the system must pass through a state whose energy is **greater** than that of the initial reactants. The activation energy is a measure of this barrier.
- The effect of temperature on reaction rate is given by the Arrhenius equation

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

المعادلة يلي اخذناها فوق
هاي نفسها

Where

K: specific reaction rate constant

A: constant called frequency factor

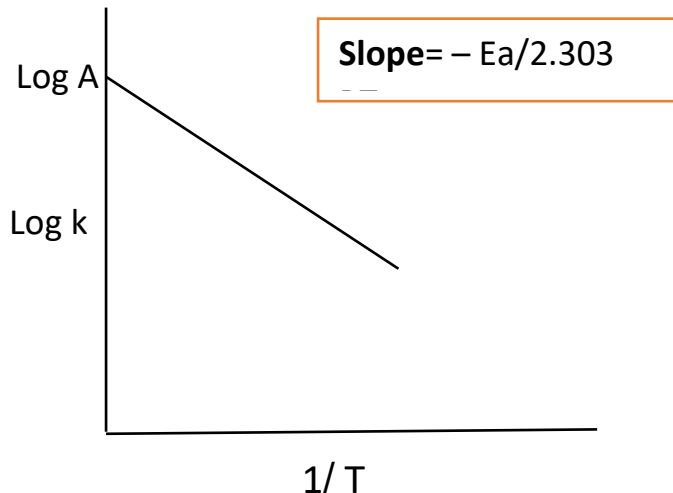
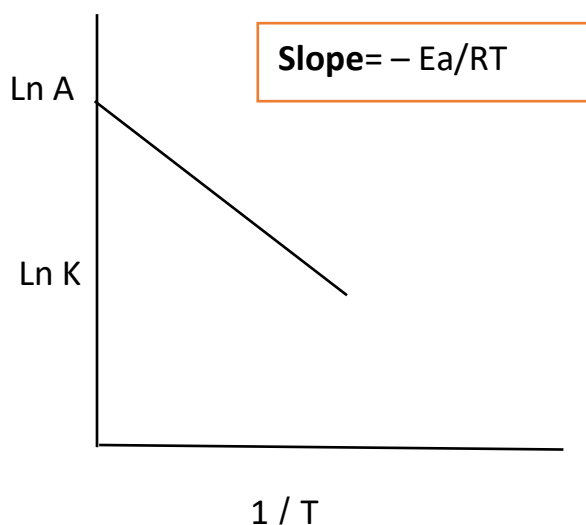
E_a: energy of activation (cal mol⁻¹ or J mol⁻¹)

R: gas constant (1.987 cal deg⁻¹ mol⁻¹; 8.314 J deg⁻¹ mol)

T: temperature (K)

$$\ln k = \ln A - E_a/RT$$

$$\log k = \log A - E_a/2.303 RT$$



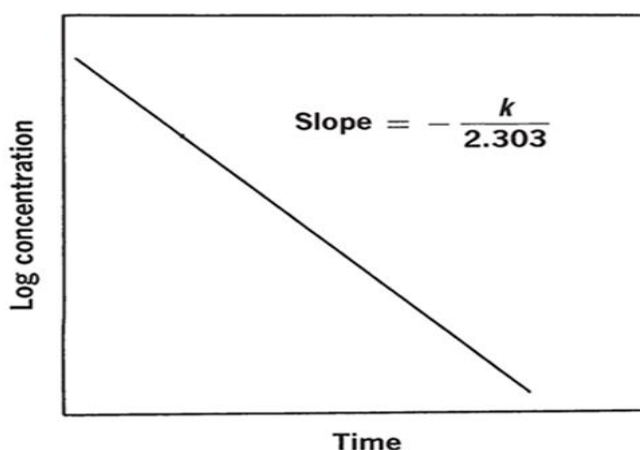
خلينا نسمي هذول الرسمتين: الرسمتين
العظيمات لانه مهمين ومنطلع منهم ال E_a

Accelerated Stability Studies

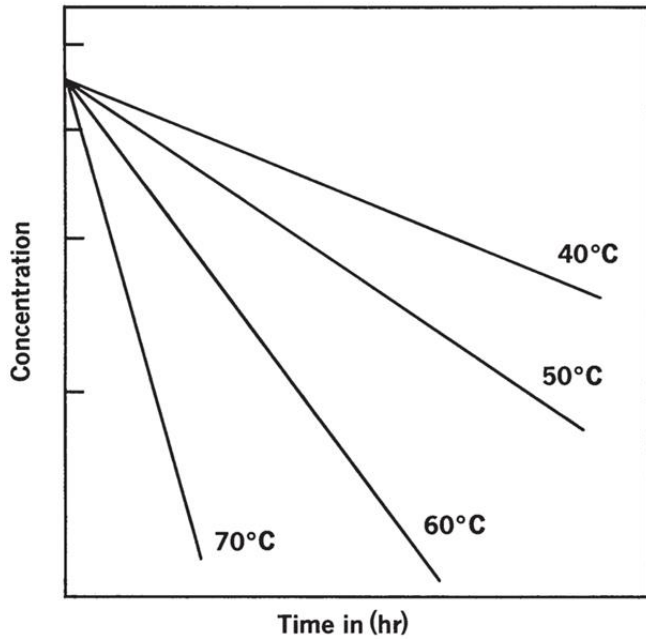
- The conventional evaluation of the stability of pharmaceutical products would require storage for a time period corresponding to the **shelf-life of the product**. This would be both time consuming and expensive. Accelerated stability studies can be performed using the principles of chemical kinetics.
- These are designed to study the rate of chemical degradation or physical change of a drug substance or drug product by using exaggerated storage conditions.

هسا زمان كانو مشان يعرفو ال stability تاعت الدوا كانو يضلهم يستنوا لحد ما يخلص ال shelf life اله وهاد الاشئ كثير بيوجد وقت ، فهسا صارو يستخدمو ال Kinetics مشان يسرعو التفاعل ويختصرو وقت ويدرسو ال stability للادوية.

- Drug solutions of known concentrations are stored at various elevated temperatures. The concentration of drug remaining undecomposed in solution is determined as a function of time. For a drug undergoing **first-order** decomposition, a plot of concentration (logarithmic scale) against time would be linear. The value of the first-order rate constant can be obtained from the slope of these lines



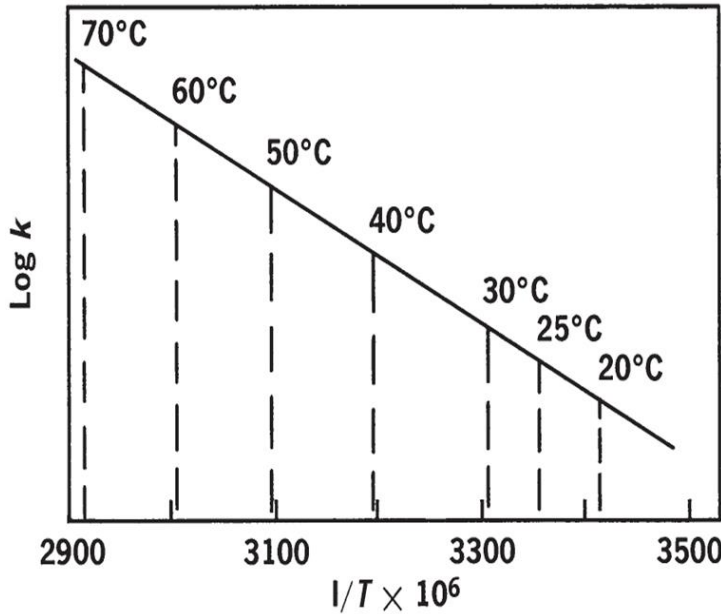
اخذناه بالبارت الماضي لما يكون log conc مع ال time وتطلع العلاقة linear بكون التفاعل first order



- لو نشوف هون كيف المادة على درجات حرارة مختلف بصيرلها degradation وشوفو كيف عند درجة الحرارة العالية 70 صار degradation اسرع مقارنة بدرجة 40
- هون الميل بساوي $-k/2.303$

- From the Arrhenius equation $\log k = \log A - E_a/2.303RT$, a plot of the decomposition rate constant (logarithmic scale) against $1/T$ should be linear.

نفس الحكي يلي فوق



- العلاقة بين $\log k$ و $1/T$ الحرارة بالكلفن اعطتنا هاد الخط المستقيم يلي ميله

$$- E_a/2.303 RT$$

- 25° هي الحرارة يلي بصير للدوا degradation بطريقة طبيعية بس بعدين لما نرفع درجة الحرارة اكثر بصير degradation اسرع
- هون ال intercept مو $\log A$ زي دايمنا لانه الخط ببيننا تغير التركيز باختلاف درجات الحرارة.
- من الرسمة منطلع k ومنعوضها بهاد القانون

$$\log k = \log A - E_a/2.303RT$$

كيف منطلع k من الرسمة؟؟

عنا قيمة حرارة منحولها للكلفن زي الرسمة ومنضربها ب 10^6 ومناخذ مقلوبها، هيك صارت زي الرسمة بالزبط، وبعدين منشوف تقاطع محور الصادات ومن $\log k$ منطلع k

- The resulting straight line can be extrapolated to **25°C** (room temperature) or to any other desired temperature. This extrapolated rate constant, **k** at 25°C, provides a measure of the stability under shelf-life conditions.
- Drug chemical decomposition pathway
 - ✓ Hydrolysis
 - ✓ Oxidation
 - ✓ Photolysis

Example 1

The rate constants for decomposition of drug were measured at five different temperatures. The data are shown below. Plot $\ln k$ versus $1/T$ and, determine the activation energy (in Kcal. /mole) for the reaction.

k (1/MS)	T (K)
3.52×10^{-7}	283
3.02×10^{-5}	356
2.19×10^{-4}	393
1.16×10^{-3}	427
3.95×10^{-2}	508

Solution:

From the given data we obtain

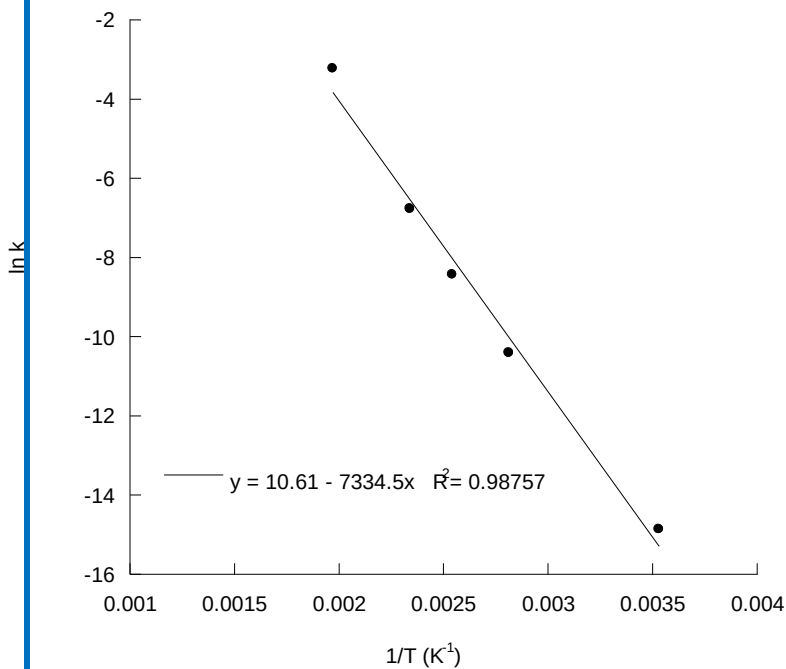
$\ln k$	$1/T$ (K ⁻¹)
-14.86	0.00353
-10.41	0.00281
-8.43	0.00254
-6.76	0.00234
-3.23	0.00197

من الجدول يلي فوق اخذنا مقلوب الحرارة و اخذنا $\ln k$ ومنعملهم رسم بياني، وهيك بكون الميل

-Ea/RT

**** ارجعو للرسمتين العظيمات**

****بهاد السؤال الجدول تاع $\ln k$ والرسم البياني والمعادلة جاهزين ونحن بس تطبيق مباشر على ال slope**



Note: when the unit is kcal
R value=1.9872 cal/deg

Slope = - 7334.5 deg

Finally, calculate the activation energy from the slope

The slope (m)= -Ea/R

$$\begin{aligned}
 E_a &= -R \cdot m = -1.9872 \text{ cal/deg mole} \times -7334.5 \text{ deg} \\
 &= 14575 \text{ cal/mole} \\
 &= 14.575 \text{ Kcal/mole}
 \end{aligned}$$

Example 2

The rate constant of a first-order reaction is $3.46 \times 10^{-2} \text{ s}^{-1}$ at **298K**. What is the rate constant at **350 K** if the activation energy for the reaction is **50.2 kJ/mole**?

Solution:

$$\ln \frac{k_2}{k_1} = \frac{E_a}{R} \left(\frac{T_2 - T_1}{T_2 T_1} \right)$$

المعادلة جديدة علينا بس
سهلة احفظوها وتطبيق
مباشر

$$\ln \frac{K_2}{3.46 \times 10^{-2}} = \frac{50.2 \times 10^3 \text{ J/mol}}{8.314 \text{ J/Kmol}} \frac{(350 \text{ K} - 298 \text{ K})}{(350 \text{ K}) * (298 \text{ K})}$$

$$K_2 = 0.702 \text{ s}^{-1}$$

Example 3

The catalytic decomposition of hydrogen peroxide can be followed by measuring the volume of oxygen liberated in a gas burette. From such an experiment, it was found that the concentration of hydrogen peroxide remaining after **65 min**, expressed as the volume in milliliters of gas evolved, was **9.60** from an initial concentration of **57.90**.

(a) Calculate k assuming **first order kinetics**.

(b) How much hydrogen peroxide remained undecomposed after **25 min**?

Solution:

a) $C_t = 9.60$

$C_0 = 57.90$

First order so we use this equation:

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

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

$$\ln (C_0/C) = kt$$

$$\ln (57.9/9.6) = k (\text{min}^{-1}) \times 65 \text{ min}$$

$$k = \ln (57.9/9.6)/65 \text{ min} = \mathbf{0.0276 \text{ min}^{-1}}$$

b)

after 25 minutes:

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

$$\begin{aligned} \ln C &= \ln 57.9 - (0.0276 \text{ min}^{-1}) (25 \text{ min}) \\ &= 3.37 \end{aligned}$$

$$\mathbf{C = 29.04}$$

Example 4

A solution of a drug contained **500 units/mL** when prepared. It was analyzed after **40 days** and was found to contain **300 units/mL**. Assuming the decomposition is **first order**, at what time will the drug have decomposed to one half of its original concentration?

Solution:

from the first order equation we find k value

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

$$\ln 300 \text{ unit/ml} = \ln 500 \text{ unit/ml} - k (40 \text{ days})$$

$$k = (\ln (500/300))/40\text{days} = 0.0128 \text{ day}^{-1}$$

ومنعوض k بقانون ال half life

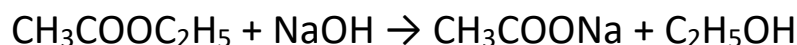
$$t_{1/2} = 0.693/k$$

$$= 0.693/0.0128 \text{ day}^{-1}$$

$$= \mathbf{54.3 \text{ days}}$$

Example 5

Walker investigated the **saponification** of ethyl acetate at 25°C:



The initial concentrations of both ethyl acetate and sodium hydroxide in the mixture were **0.01000 M**. The change in concentration, x, of alkali during **20 min** was 0.000566 mole/liter; therefore, $(a-x) = 0.01000 - 0.000566 = 0.009434$.

Compute (a) the rate constant and

(b) the half-life of the reaction

Solution:

*Keep in mind: saponification means **second order reaction**, and since the reactants are different it is **type 1**

$$\frac{x}{a(a-x)} = kt$$

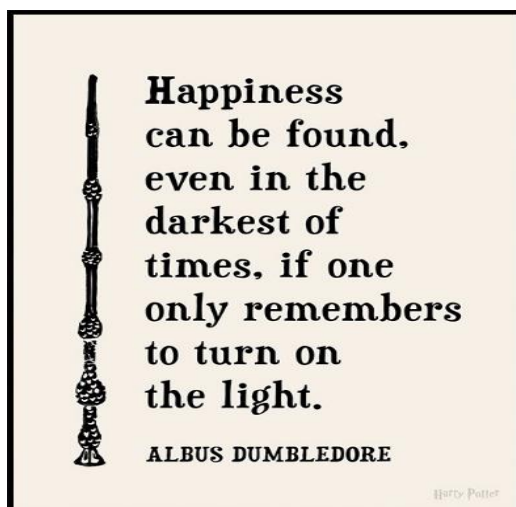
$$\frac{0.00566 \text{ mol / L}}{0.01(0.01000 - 0.00566)} = k(20 \text{ min})$$

$$k = 6.52 \text{ L mol}^{-1}\text{min}^{-1}$$

$$t_{1/2} = 1/ak$$

$$= 1/(0.01 \text{ mol/L}) (6.52 \text{ L mol}^{-1}\text{min}^{-1})$$

$$= 15.3 \text{ min}$$



Kinetics part 2 DONE

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