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Research Article

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Kinetics Study of Reaction between Atenolol Epoxide and Isopropylamine using Differential and Integral Method of Analysis

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Abstract In this paper Differential and Integral method of analysis of data for Batch reactor is used to find the rate and order of reaction of Atenolol. These both methods are useful for fitting simple chemical reactions. The concentration of the product and reactants are calculated from the simple method of acid-base titration. In Differential method of analysis, experimental data for the reactant are plotted as a function of reaction time. A smooth curve is drawn through these data, and tangents are drawn to the curve at various points. The slope of each one of these tangents gives the instantaneous reaction rate. These rates are then plotted versus concentration of the species being followed on a log-log scale. The slope of the line formed gives the reaction order with respect to this reactants. Integral method puts a particular rate equation to test by integrating and comparing the predicted C versus t curve with experimental C versus t data. If the fit is unsatisfactory, another rate equation is tested. The key raw materials required to produce Atenolol epoxide are Atenolol epoxide and Monoisopropylamine (MIPA). Firstly, the order and rate with respect to reactant *i.e.* Atenolol epoxide is tested and then overall order and rate of equation is evaluated with Differential and Integral method of analysis of data. The integrated rate law depends on the kinetics. Since the reaction is being carried out in a batch reactor, the volume of reactor is assumed constant throughout the reaction.

Keywords Differential method of analysis, Instantaneous reaction rate, Curve fitting, Rate Equation

Introduction

Reaction:-Atenolol epoxide + Isopropyl amine → Atenolol

The rate at which reaction occurs will depend on the concentration of Atenolol epoxide and Monoisopropylamine (MIPA) in the reaction mass and temperature. In order for a molecule of Atenolol epoxide and a molecule of Monoisopropylamine (MIPA) to combine to form Atenolol, the two molecules must come into contact with each other (contact meaning approach within a certain distance so that bonding forces can play a role) [1]. The experiments are selected to be performed at isothermal conditions so that the rate's dependence on concentrations is established. The concentration of the product and reactants are calculated from the simple method of acid-base titration as atenolol is base it reacts with hydrochloric acid forms salt and water. In a titration, measured amounts of acid and base combine to produce a salt and water. If the salt formed is soluble in water, no precipitate is formed. To determine the endpoint of the titration, a small amount of indicator is added to the reaction mixture. A titration is based on the molar relationship between H^+ (or H_3O^+) and OH ions reflected in the balanced equation of an acid-base reaction. When the endpoint of the titration is reached, the number of H_3O^+ ions is equivalent to the number of OH ions. There are two methods for analyzing kinetic data, the differential and the integral methods. Both methods are graphical method. Both methods depend on the experimental data and give the order of reaction and rate constant of reaction [2]. In Differential method of analysis, experimental data for the reactant are plotted as a function of reaction time. A smooth curve is drawn

through these data, and tangents are drawn to the curve at various points. The slope of each one of these tangents gives the instantaneous reaction rate. These rates are then plotted versus concentration of the species being followed on a log-log scale. The slope of the line formed gives the reaction order with respect to this constituent [3]. In the integral method of analysis we guess a particular form of rate equation and, after appropriate integration, predict that the plot of a certain concentration function versus time should yield a straight line. The data are plotted, and if a fairly good straight line is obtained, then the rate equation is said to satisfactorily fit the data.

The term, the constant-volume batch reactor, refer to the volume of reaction mass, and not the volume of reactor. Thus, this term particularly refers to a constant-density reaction system. The measure of reaction rate of component i, in a constant-volume system become

$$ri = \frac{1}{V}\frac{dNi}{dt} = \frac{dCi}{dt} \quad (1)$$

Thus, any component's rate of reaction is given by the rate of change of its concentration with time [3]. The fractional conversion of any reactant, say A, converted is the fraction of A reacted away, with Symbol X_A. Let the initial amount of A in the reactor at time t = 0 is N_{Ao}, and the amount present at time t is N_A. Then in constant volume system the conversion of A is

$$X_A = \frac{N_{Ao} - N_A}{N_{Ao}} = 1 - \frac{C_A}{C_{Ao}} \quad (2)$$

Comparison of the methods

For this power-law rate equation, it is interesting to compare the integral and differential methods. The integral method requires you to separately test each guessed value of n but you don't have to differentiate the data. The differential method allows you to determine k and n from one plot but, in order to get that plot, you have to process - differentiate - the data [3]. You should know how to do both methods. If you have a new reaction with an unknown rate equation, you may be able to propose a rate equation from your knowledge of the chemistry. Then you might have luck using the integral method. For complex reaction kinetics, it might be advisable to use the differential method to see how the rate depends on the concentrations of the different components in the reaction mixture. Here we use an example where only C_A affects the rates but, in general, there may be more components involved in a rate equation.

Materials and Methods

I. Differential method of kinetic data analysis

In this method, we collect concentration vs. time data, e.g., C_A vs. Rate of reaction, and then differentiate the data [3]. That is, determine the slopes dC_A/dt (or dX_A/dt) at a series of different times. At each of these times, we have measurements (or interpolated measurements) of fluid composition, e.g., C_A.

For a constant volume, isothermal batch reactor

$$r_A = \frac{dC_A}{dt} \quad (3)$$

So we now have estimates of the reaction rate at known compositions. For example, we have a table of r_A and C_A values. The next step is to find a rate function that can fit the data. A special case is the power-law rate equation. For an essentially irreversible reaction of order n,

$$r_A = kC_A^n \quad (4)$$

$$\ln(r_A) = \ln(k) + n*\ln(C_A) \quad (5)$$

Plot points of $\ln(r_A)$ vs. $\ln(C_A)$ then fit a straight line through the points to get ln(k) and the order n [3].

II. Integral method of analysis of data

In this method, we start with the functional form of a rate equation. The rate equation may be given to us, or we propose a functional form ourselves, e.g., first-order or second-order. Then we put the rate equation into the balance equation and integrate the balance equation. Finally, we determine if the integrated equation can "fit the

data" and, if it does fit, determine the values of the rate coefficients. By "fit the data" we mean that the rate equation can predict the how the experimental data change as reaction time or initial concentrations are changed [1].

A. 1st-order rate equation and integral method

First let's look at a 1st-order reaction. We may already know the reaction is 1st order but not know the value of the rate coefficient, or we may propose this rate equation if we don't know the equation. The reaction is either essentially irreversible, or we take data at early times such that the back rate is negligible. Specify that we have obtained a table of time and C_A values.

$$dN_A/dt = r_{A*}V = -kC_{A*}V \quad (6)$$

Here specify a constant volume reactor.

$$dC_A/dt = -k*CA \quad (7)$$

$$t=0 ; C_A(0)=C_{A0}$$

$$-\ln(CA/C_{A0})=k*t \quad (8)$$

Now test to see if this fits the data by plotting -ln(CA/CA0) = -ln(1 - XA) for constant V, vs. time. If the data points fall along a straight line, then we can conclude that a 1st-order rate equation fits the data. The slope of a line fit through the data has a slope equal to the value of k [3].

B. 2nd-order rate equation and integral method

Specify a constant volume reactor.

$$dC_A/dt = -kC_A^2 \quad (9)$$

$$t=0; CA(0)=C_{A0}, \text{Integrate}$$

$$(1/C_A - 1/C_{A0})=k*t \quad (10)$$

Now test to see if this fits the data by plotting $(1/C_A - 1/C_{A0})$ vs. time. If the data points fall along a straight line, then we can conclude that a 2nd-order rate equation fits the data. The slope of a line fit through the data has a slope equal to the value of k [3].

C. For the reaction,

$$A+B \rightarrow R$$

$$\frac{(C_{A0}-C_{BO})(C_{B0}-C_B)}{C_{B0}C_B}+\ln\left(\frac{C_BC_{A0}}{C_AC_{B0}}\right)=(C_{B0}-C_{A0})^2kt \quad (11)$$

D. Experimental Data and Calculation:

i. Atenolol Titration Data for Order with Atenolol epoxide:

Table 1: General parameter for trial 01 with epoxide

Trial no.	01
Room temp.	32 ºC
Sample quantity(Z)	5 mL
Indicator	Bromothylmol Blue
End point	Blue to yellow colour change
Atenolol epoxide initial molarity(mol/L)	3.295
HCl molarity(mol/L)(x)	1
MIPA molarity (mol/L)	10.83

Table 2: Titration reading for trial 01 with epoxide

Sample No.	**Burette reading (mL)**		**Difference (y)**
	Initial	**Final**	
1	27	20.9	6.1
2	27	17.6	9.4
3	27	14.5	12.5
4	27	12.8	14.2
5	27	12.2	14.8
6	27	11.6	15.4
7	27	11.1	15.9
8	27	10.9	16.1

Calculation :-

Atenolol molarity=x*y/z=1*y/5=0.2*y

From reaction,Atenolol epoxide reacted=Atenolol formed

Atenolol epoxide unreacted=Atenolol epoxide initial - Atenolol epoxide reacted

Table 3: Calculation of epoxide concentration foe trial 01

Sample No.	Time (hr.)	Atenolol (mol/L)	Atenolol epoxide (mol/L)
-	0	0	3.295
1	1	1.22	2.075
2	2	1.88	1.415
3	3	2.5	0.795
4	4	2.84	0.455
5	5	2.96	0.335
6	6	3.08	0.215
7	7	3.18	0.115
8	8	3.22	0.075

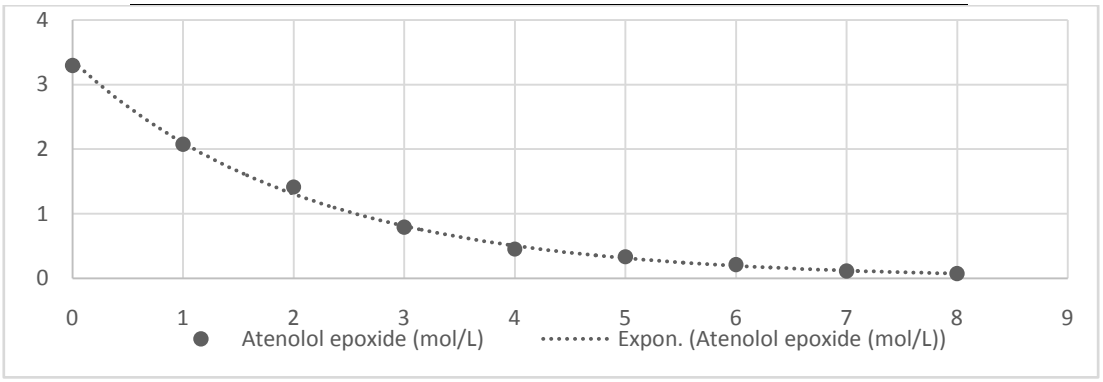

Figure 1: Concentration of epoxide v/s time curve for trial 01

From above graph, concentration v/s rate of reaction with epoxide table is obtained as follow:-

Table 4: Concentration of epoxide v/s rate of reaction with epoxide for trial 01

Atenolol epoxide (mol/L)	Ln (Conc.)	Rate of reaction	Ln (rate)
3.295	1.192	1.22	0.199
2.075	0.730	0.66	-0.416
1.415	0.347	0.62	-0.478
0.795	-0.229	0.34	-1.079
0.455	-0.787	0.12	-2.120
0.335	-1.094	0.12	-2.120
0.215	-1.537	0.1	-2.303
0.115	-2.163	0.04	-3.219

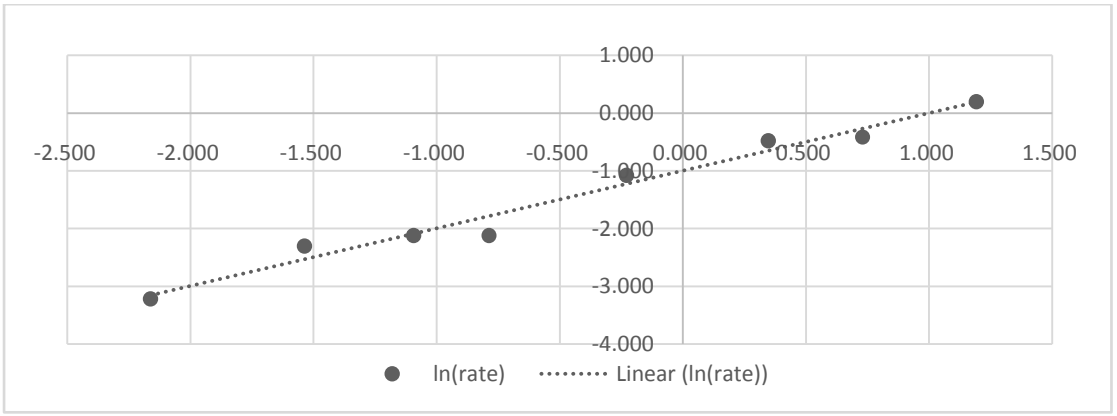

Figure 2: Ln(rate) v/s Ln(concentration) curve with epoxide for trial 01

From above graph and equation (5),

Order with epoxide= α = Slope of above curve =1
Ln(k) = y-intercept of above curve =-1.0158
Hence, k =0.3621 (1/hr)

Table 5: Integral analysis data for trial 01 with epoxide

Time (hr)	Atenolol epoxide (mol/L)	Ln (C_{A0}/C_A)
0	3.295	0.000
1	2.075	0.462
2	1.415	0.845
3	0.795	1.422
4	0.455	1.980
5	0.335	2.286
6	0.215	2.730
7	0.115	3.355
8	0.075	3.783

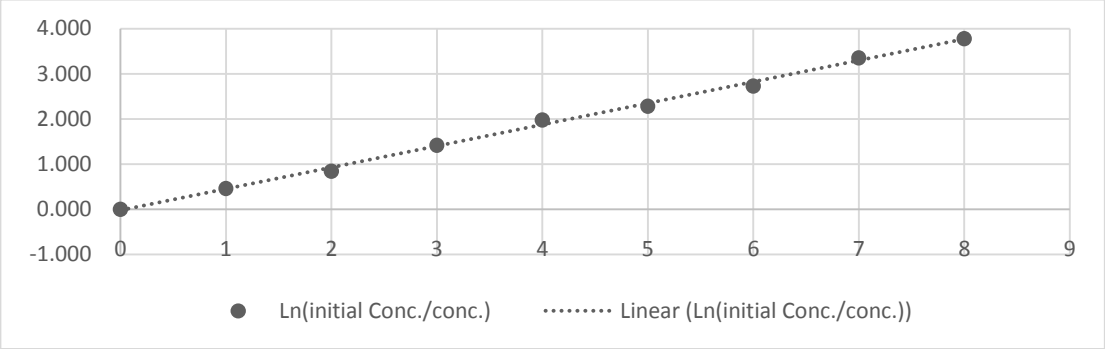

Figure 3: Ln(CA0/CA) v/s Time(hr.) curve with epoxide for trial 01

From, above graph and equation (8),
Order of reaction with respect to epoxide =1.0
k = Slope of above curve =0.3728 (1/hr)

Table 6: General parameter for trial 02 with epoxide

Trial no.	02
Room temp.	36 ºC
Sample quantity(Z)	5 mL
Indicator	Bromothylmol Blue
End point	Blue to yellow colour change
Atenolol epoxide initial molarity(mol/L)	3.295
HCl molarity(mol/L)(x)	1
MIPA molarity (mol/L)	10.83

Table 7: Titration readings for trial 02 with epoxide

Sample No.	Burette reading (mL)		Difference (y)
	Initial	Final	
1	27	19.5	7.5
2	27	18.4	8.6
3	27	15.1	11.9
4	27	12.5	14.5
5	27	12.2	14.8
6	27	11.4	15.6
7	27	11.2	15.8
8	27	10.9	16.1

Table 8: Calculation of epoxide concentration for trial 02

Sample No.	Time (hr.)	Atenolol (mol/L)	Atenolol epoxide (mol/L)
-	0	0	3.295
1	1	1.5	1.795
2	2	1.72	1.575
3	3	2.38	0.915
4	4	2.9	0.395
5	5	2.96	0.335
6	6	3.12	0.175
7	7	3.16	0.135
8	8	3.22	0.075

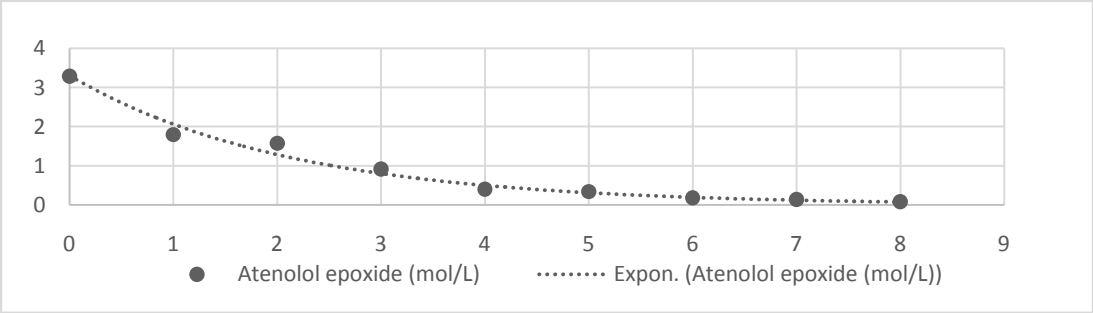

Figure 4: Concentration v/s Time curve with epoxide for trial 02

From above graph, concentration v/s rate table is obtained as follow:-

Atenolol epoxide (mol/L)	Ln(Conc.)	Rate of reaction	ln (rate)
3.295	1.192	1.5	0.405
1.795	0.585	0.22	-1.514
1.575	0.454	0.66	-0.416
0.915	-0.089	0.52	-0.654
0.395	-0.929	0.06	-2.813
0.335	-1.094	0.16	-1.833
0.175	-1.743	0.04	-3.219
0.135	-2.002	0.06	-2.813

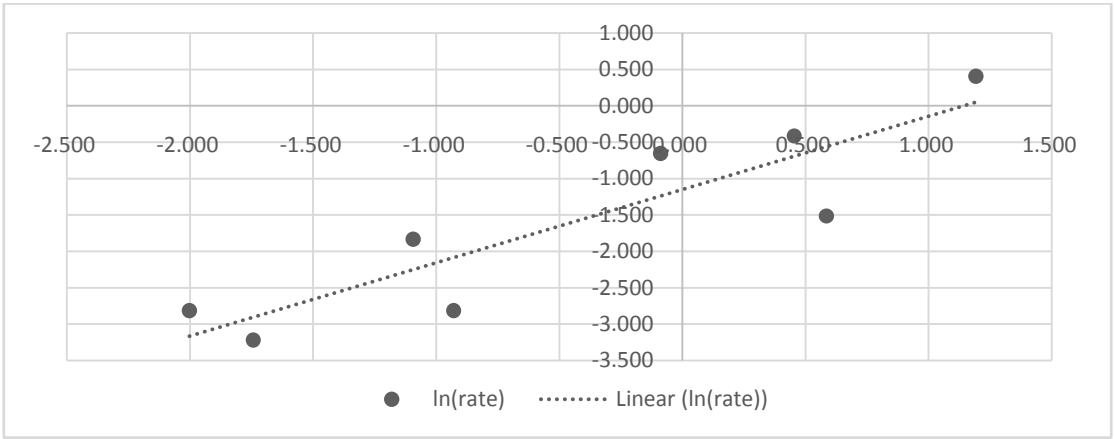

Figure 5: Ln(rate) v/s Ln(concentration) curve with epoxide for trial 02

From above graph and equation (5),

Order with epoxide= α = Slope of above curve =1

Ln(k) = y-intercept of above curve =-1.0130
Hence, k =0.3631 (1/hr)

Table 9: Integral analysis data with epoxide for trial 02

Time(hr)	Atenolol epoxide (mol/L)	$Ln(C_{A0}/C_A.)$
0	3.295	0.000
1	1.795	0.607
2	1.575	0.738
3	0.915	1.281
4	0.395	2.121
5	0.335	2.286
6	0.175	2.935
7	0.135	3.195
8	0.075	3.783

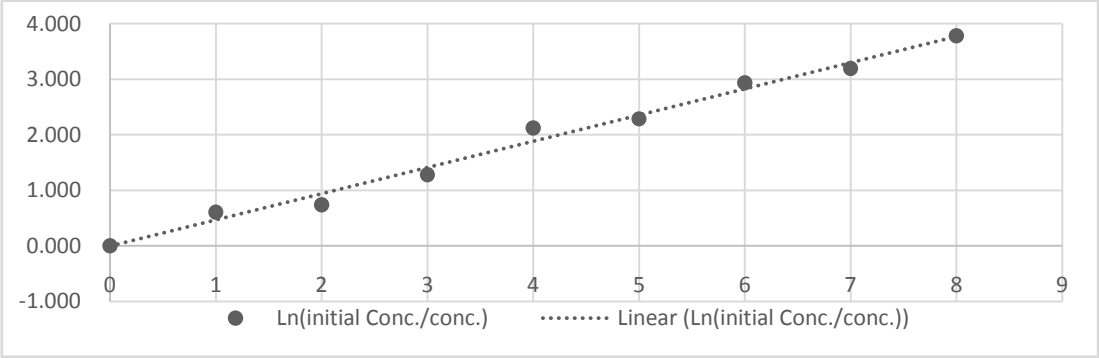

Figure 6: $Ln(C_{A0}/C_A.)$ v/s Time curve with epoxide for trial 02

From above graph and equation (8),
Order of reaction with respect to epoxide =1.0
k = Slope of above curve =0.3728 (1/hr)
Hence, K_{avg}=0.3704 hr^{-1}
$-r_A=0.3704*C_A$

ii. Atenolol Titration Data for Order with Isopropyl amine (MIPA):-

Table 10: General parameter for trial 01 with MIPA

Trial no.	01
Room temp.	34 ºC
Sample quantity (Z)	5 mL
Indicator	Bromothylmol Blue
End point	Blue to yellow colour change
Atenolol epoxide initial molarity (mol/L)	20
HCl molarity (mol/L)(x)	2.5
MIPA initial molarity (mol/L)	10.83

Table 11: Titration readings for trial 01 with MIPA

Sample No.	Burette reading (mL)		Difference (y)
	Initial	Final	
1	27	17.7	9.3
2	27	14.4	12.6
3	27	9.6	17.4
4	27	7.5	19.5
5	27	6.7	20.3
6	27	6.2	20.8
7	27	5.9	21.1
8	27	5.7	21.3

Calculation:-

Atenolol molarity=x*y/z=2.5*y/5=0.5*y

From reaction,MIPA reacted=Atenolol formed

MIPA unreacted=MIPA initial - MIPA reacted

Table 12: Calculation of concentration of MIPA for trial 01

Sample No.	Time (hr.)	Atenolol (mol/L)	MIPA (mol/L)
-	-	0	10.83
1	1	4.650	6.180
2	2	6.300	4.530
3	3	8.700	2.130
4	4	9.750	1.080
5	5	10.150	0.680
6	6	10.400	0.430
7	7	10.550	0.280
8	8	10.650	0.180

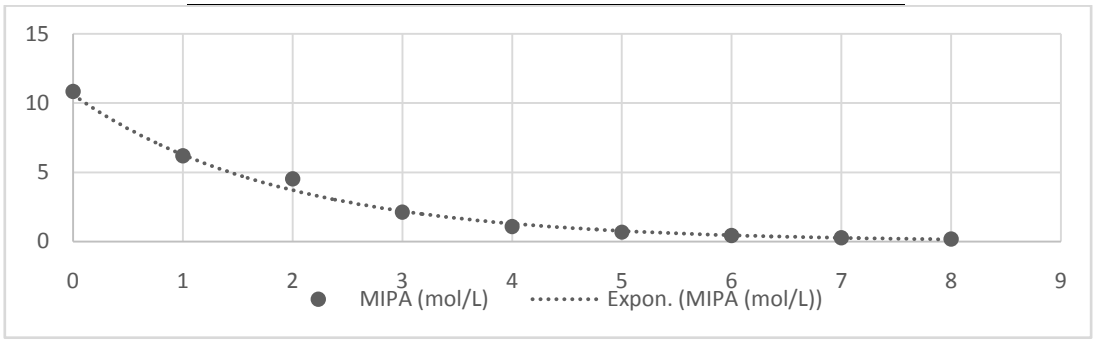

Figure 7: MIPA (mol/L) v/s time(hr) curve for trial 01

From above graph, concentration v/s rate table is obtained as follow:-

Table 13: Concentration v/s rate with MIPA for trial 01

MIPA (mol/L)	Ln(Conc.)	Rate of reaction	ln(rate)
10.83	2.382	4.65	1.537
6.18	1.821	1.65	0.501
4.53	1.511	2.4	0.875
2.13	0.756	1.05	0.049
1.08	0.077	0.4	-0.916
0.68	-0.386	0.25	-1.386
0.43	-0.844	0.15	-1.897
0.28	-1.273	0.1	-2.303

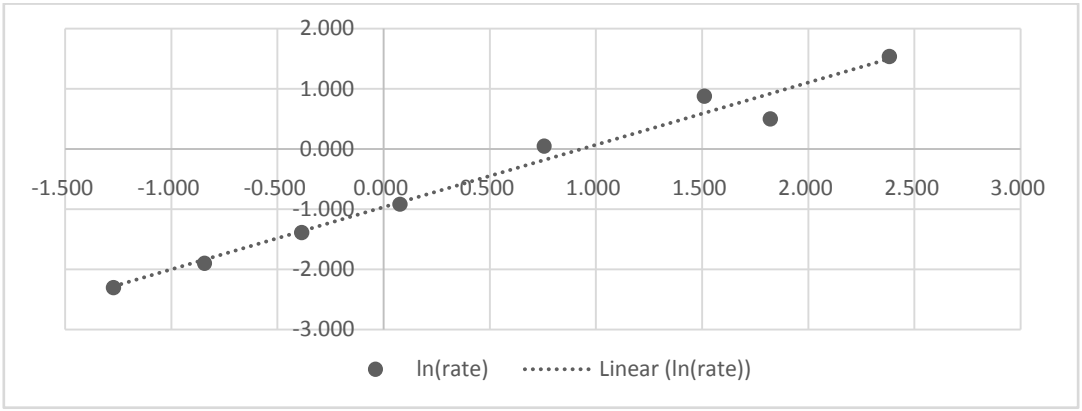

Figure 8: ln(rate) v/s ln(concentration of MIPA) for trial 01

From above graph and equation (5),
Order with MIPA = β = Slope of above curve =1.0
Ln(k) = y-intercept of above curve =-0.6780
Hence, k=0.5076 (1/hr)

Table 14: Integral analysis data for trial 01 with MIPA

Time(hr)	MIPA(mol/L)	$Ln(C_{B0}/C_B)$
0	10.83	0.000
1	6.18	0.561
2	4.53	0.872
3	2.13	1.626
4	1.08	2.305
5	0.68	2.768
6	0.43	3.226
7	0.28	3.655
8	0.18	4.097

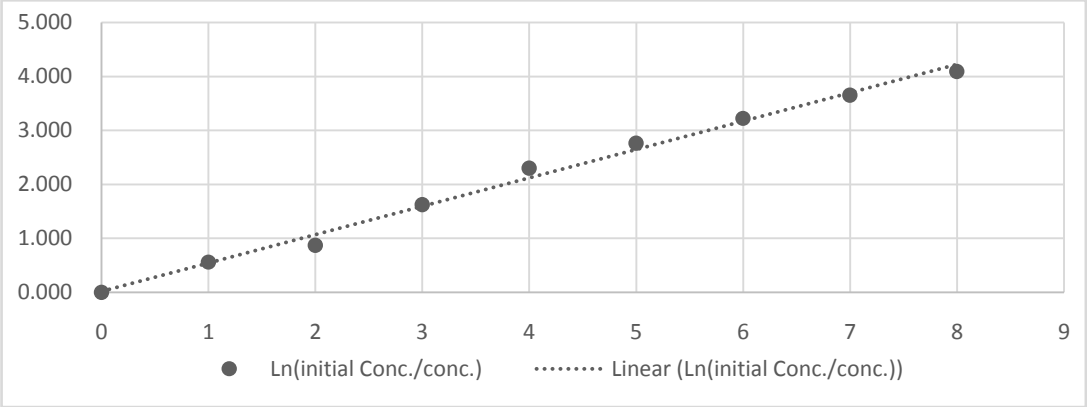

Figure 9: Ln(CB0/CB) v/s time(hr) curve with MIPA for trial 01

From above graph and equation (8),
Order of reaction with respect to MIPA =1.0
k = Slope of above curve =0.5076 (1/hr)

Table 15: General parameter for trial 02 with MIPA

Trial no.	02
Room temp.	36 ºC
Sample quantity(Z)	5 mL
Indicator	Bromothylmol Blue
End point	Blue to yellow colour change
Atenolol epoxide initial molarity(mol/L)	20
HCl molarity(mol/L)(x)	2.5
MIPA initial molarity (mol/L)	10.83

Table 16: Burette reading for trial 02 with MIPA

Sample No.	Burette reading (mL)		Difference (y)
	Initial	Final	
1	27	17.4	9.6
2	27	11.9	15.1
3	27	9.12	17.88
4	27	7.5	19.5
5	27	6.5	20.5
6	27	6	21
7	27	5.7	21.3
8	27	5.6	21.4

Table 17: Calculation of MIPA concentration for trial 02

Sample No.	Time (hr.)	Atenolol (mol/L)	MIPA (mol/L)
-	0	0	10.83
1	1	4.800	6.030
2	2	7.550	3.280
3	3	8.940	1.890
4	4	9.750	1.080
5	5	10.250	0.580
6	6	10.500	0.330
7	7	10.650	0.180
8	8	10.700	0.130

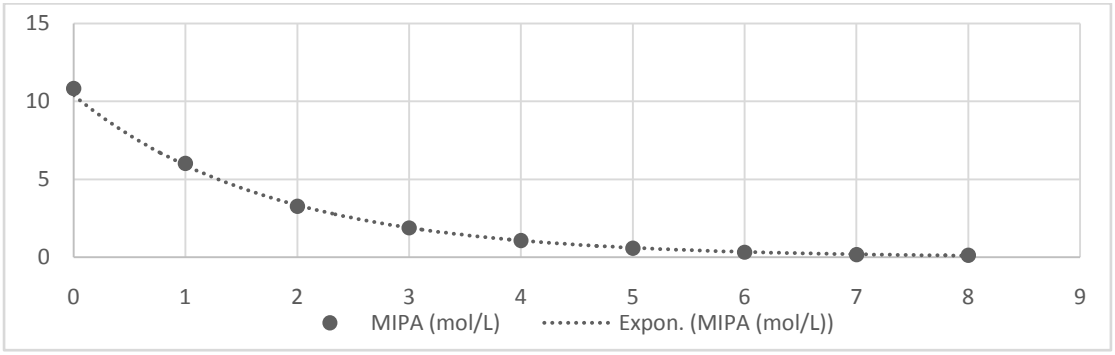

Figure 10: Concentration of MIPA v/s time curve for trial 02

From above graph, concentration v/s rate table is obtained as follow:-

Table 18: Concentration of MIPA v/s Rate for trial 02

MIPA (mol/L)	Ln(Conc.)	Rate of reaction	ln(rate)
10.83	2.382	4.800	1.569
6.03	1.797	2.750	1.012
3.28	1.188	1.390	0.329
1.89	0.637	0.810	-0.211
1.08	0.077	0.500	-0.693
0.58	-0.545	0.250	-1.386
0.33	-1.109	0.150	-1.897
0.18	-1.715	0.050	-2.996

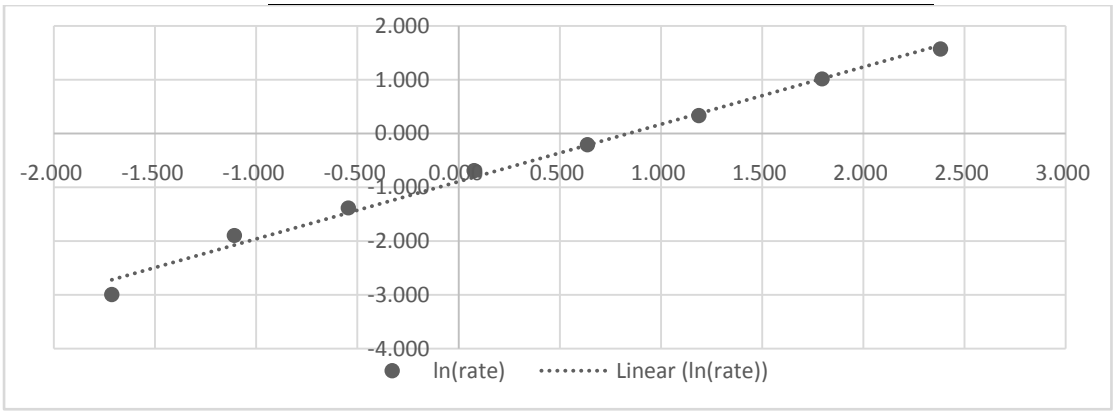

Figure 11: ln(rate) v/s ln(concentration of MIPA) curve for trial 02

From, above graph and equation (5),

Order with MIPA = β = Slope of above curve =1.0

Ln(k) = y-intercept of above curve =-0.6780

Hence, k =0.5076 (1/hr)

Table 19: Integral analysis data for trial 02 with MIPA

Time(hr)	MIPA(mol/L)	LnC_{B0}/C_B.)
0	10.83	0.000
1	6.03	0.586
2	3.28	1.194
3	1.89	1.746
4	1.08	2.305
5	0.58	2.927
6	0.33	3.491
7	0.18	4.097
8	0.13	4.423

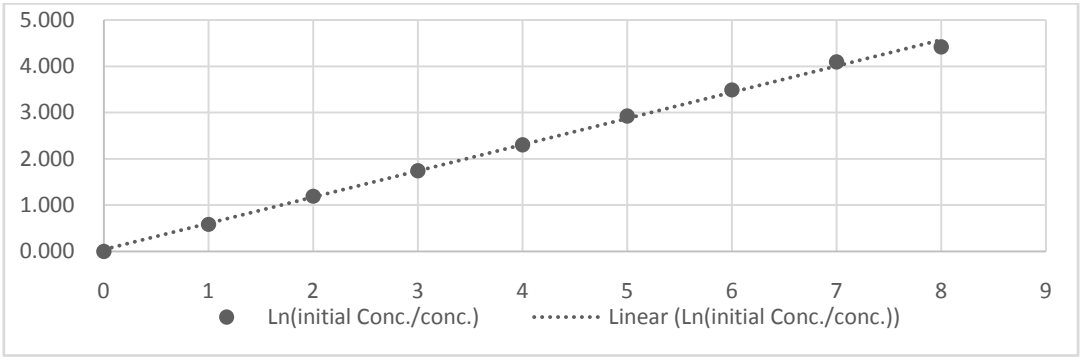

Figure 12: Ln(CB0/CB) v/s time(hr) curve for trial 02

From above graph and equation (8),

Order of reaction with respect to MIPA =1.0

k =Slope of above curve =0.5076 (1/hr)

Hence, k_{avg}=0.5076 hr^{-1}

$-r_B = 0.5076 * C_B$

iii. Atenolol Titration Data for Overall Order:-

Table 20: General parameter for overall arder

Room temp.	35ºC
Sample quantity(Z)	5 mL
Indicator	Bromothylmol Blue
End point	Blue to yellow colour change
Atenolol epoxide initial molarity(mol/L)	3.295
HCl molarity(mol/L)(x)	2.5
MIPA initial molarity (mol/L)	10.83

Table 21: Burette readings for overall order

Sample No.	Burette reading (mL)		Difference (y)
	Initial	Final	
1	27	25.5	1.5
2	27	24.6	2.4
3	27	23.5	3.5
4	27	22.4	4.6
5	27	21.5	5.5
6	27	21	6
7	27	20.8	6.2
8	27	20.5	6.5

Calculation:-

Atenolol molarity=x*y/z=2.5*y/5=0.5*y

From reaction, Atenolol epoxide reacted =MIPA reacted=Atenolol formed

Atenolol epoxide unreacted=Atenolol epoxide initial - Atenolol epoxide reacted

MIPA unreacted=MIPA initial - MIPA reacted

Table 22: Calculation concentration of epoxide and MIPA for overall order

Time(hr)	Sample No.	Atenolol (mol/L)	Atenolol epoxide (mol/L)	MIPA (mol/L)	$\ln(\frac{C_B C_{A0}}{C_A C_{B0}})$
0	-	0.00	3.30	10.83	4.76
1	1	0.75	2.55	10.08	4.95
2	2	1.20	2.10	9.63	5.10
3	3	1.75	1.55	9.08	5.35
4	4	2.30	0.99	8.53	5.72
5	5	2.75	0.55	8.08	6.27
6	6	3.00	0.30	7.83	6.85
7	7	3.10	0.20	7.73	7.25
8	8	3.25	0.04	7.58	8.70

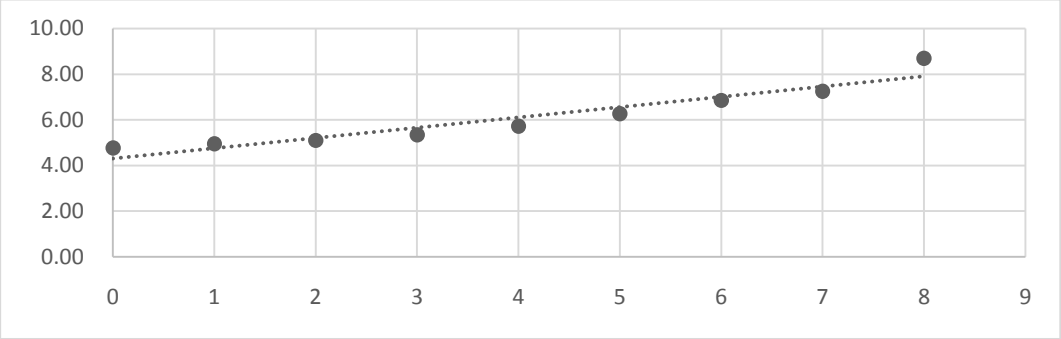

Figure 13: ln((CB0CA)/(CA0CB)) v/s time curve

From above graph and equation (11),

Slope of curve=0.805= $(C_{B0}-C_{A0})^2$*k

Hence, k=0.014

Hence,-r=0.014C_AC_B

Conclusion

By above two methods, it is proved that the overall order of reaction is two as order with each reactant is one. The reaction of Atenolol is a homogeneous reaction with no catalyst used. The concentrations versus time data are used to find the order of reaction.

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