Shireen I. Hamadamin, Kareem Sh. Ahmed, Hassan A. Mohammed / International Journal of Engineering Research and Applications (IJERA) ISSN: 2248-9622 www.ijera.com
Vol. 2, Issue6, November- December 2012, pp.1329-1336

Kinetics and thermodynamic studies of the bromination of sultams using conductivity measurement

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ABSTRACT

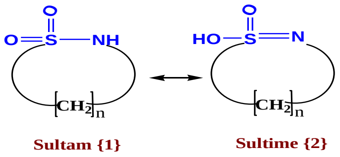
Kinetics and thermodynamic studies of bromination of (1,2-thiazine): N-(p-substituted phenyl) -3,5- dimethyl -1, 1-dioxo-1,2-thiazine ($C_4H_2(CH_3)_2SO_2$ N C_6H_4-X); {X = H, p-Cl, and p-OCH_3} by using bromine(Br_2) in chloroform medium have been investigated by Isolation method the observed rate of bromination, pseudo first order for 1,2-thiazine and Br_2 and second order in overall reaction and using conductivity measurements. The reaction rate constant increases with increasing temperature from 273K to 318K. The kinetic and thermodynamic parameters k, E_a, $\Delta H^{\#}$ and $\Delta S^{\#}$ have been calculated. The corresponding halogenated 1,2-thiazine has been identified as a product of halogenation. A suitable reaction scheme is proposed and an appropriate rate law is deduced to account for the observed kinetic and thermodynamic data.

Keywords – ***1,2-thiazine, Bromine (Br_2), Conductivity, rate constant, Sulfonamide.***

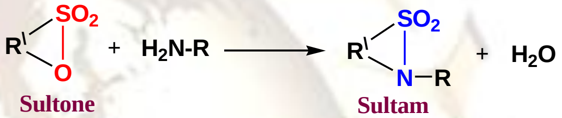
I. INTRODUCTION

Sulfonamides have long been recognized for their wide range of biological activities[1] and are among the most common causes of allergic reactions of drugs. Recently, much interest has been directed to their cyclic counterparts, the sultams, which also exhibit a vast variety of biological activities. A number of substituted sultams have proven to be useful heterocycles for medical applications[2,3]. As a consequence, chemical syntheses towards sultams have continued to be an attractive topic for intense research[4].

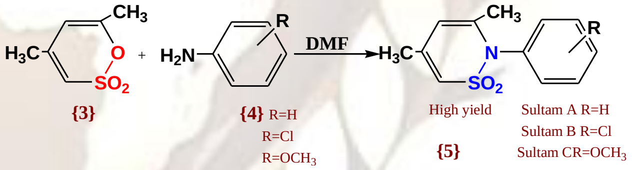
Sultams {1} are inner Sulfonamides in which the S–N bond is part of a ring, the tautomeric forms of sultams, having a sulfur–nitrogen double bond as part of a ring, are called Sultimes {2}. The chemical composition of which corresponds to the general formula[5]:



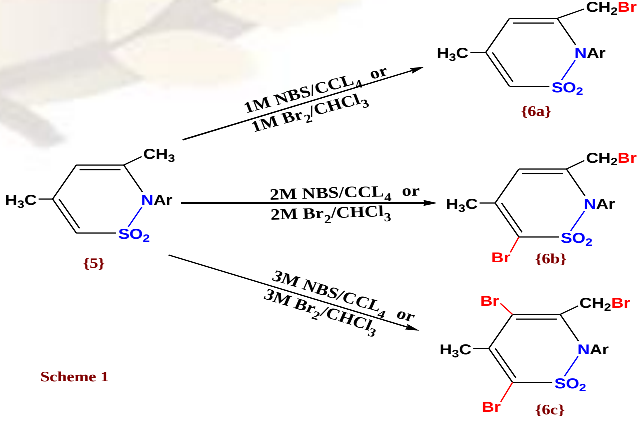
Unsaturated sultams prepared from the corresponding sultones, (Sultones are intramolecular cyclic esters of hydroxy sulfonic acids) it has surprisingly been found that unsaturated sultones may be condensed with ammonia or primary amines yielding unsaturated sultams. The reaction proceeds in accordance with the general reaction scheme[6]:



The unsaturated sultams, in accordance with the invention are highly stable and permit further reactions in the sultam ring as well as in the substituents at the sultam nitrogen atom[6]. 1,2-thiazine is a type of sultams, was prepared by mixing of 4,6-dimethyl-1,2-oxathiine-2,2-dioxide{3} with aniline {4} or p-substituted aniline and heated for 1.5 hr., giving N-(p-substitutedphenyl)-3,5-dimethyl-1,1-dioxo-1,2-thiazine {5}[7,8].



Funghanel and co-worker, used elementary bromine[9] for the bromination of 1,2-thiazine, also using different molar ratio of N-bromosuccinimide, which is high selective brominating agent to obtain the same product with higher yields[10] (scheme 1).



Scheme 1

Because of our continuing interest in mild reagents for the introducing of halogens into organic molecules and because only limited kinetic and thermodynamic information is available on sultam reactions with bromine, we found it is important to determine kinetic and thermodynamic parameters of the halogenation reactions of 1,2-thiazine.

II. EXPERIMENTAL

2.1 Chemicals

All chemicals used were of an analytical grade reagent, and methanol (99.9% purity) was purchased from TEDIA Company, Inc. (USA). N,N-Dimethylformamide (DMF) 99.8% from BioSolve. Acetone 99.5%, Chloroform >99.4%, bromine (Br_2) >97% hydrochloric acid (HCl) 97% by Fluka., Aniline 90% , Acetic anhydride 99%, Sulphuric acid and sultone 98% by Sigma Aldrich Co.,4-Chloroaniline, 4-methoxyaniline by Riedel-de Haën, Franç.

2.2 Synthesis of N-(p-substituted phenyl)-3,5-dimethyl-1,1-dioxo-1,2-thiazine ((5)A-C)

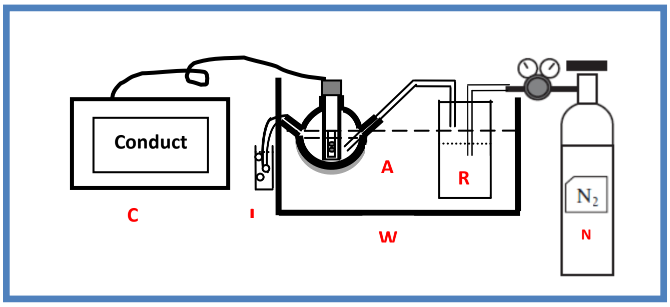
A mixture of 0.1mole (16gm) sultone {3} and 0.1 mole (9.1 ml) of aniline or p-substituted aniline were dissolved in 25ml N,N-dimethyl formamide (DMF), the contents reflexed for 1.5hr , then cooled to room temperature and 10ml of (0.1 N) HCl was added to remove the excess of aniline then the precipitate collected by filtration, washed with cold water dried and recrystallized in methanol[9]. The physical properties are shown in table(1).

Table (1): Some physical properties of the compounds (sultam A, B, C).

Compounds	***para-R***		***Molecular formula***	***M.wt g/mol.***	***Yield %***
Sultam {5}	A	H	$C_{12}H_{13}NO_2S$	235.303	53
	B	Cl	$C_{12}H_{12}NO_2SCl$	269.749	42
	C	OCH_3	$C_{13}H_{15}NO_3S$	265.329	49

2.3 Experimental techniques and apparatus

The conductivity of the dissolved hydrogen bromide was measured by Hanna conductivity meter that was readily adapted to automatic recording operation as in fig. (1) at temperatures (273, 283, 293, 298, 303, 318)K, for each temperature the conductivity was measured for a (200ml) water in a round bottom flask in which the hydrogen bromide (HBr) gas evolved as a side product of the reaction was dissolved by passing nitrogen gas flow through the reaction at different time intervals.



Figure(1):Illustrative schematic diagram of the electrical conductivity measurement.

2.3.1 Typical kinetic experiment of the molar ratio (1:15) (Sultam A : Br_2)

0.235g (0.001mol, 0.0928mol dm^{-3}) of 1,2-thiazine (Sultam A) was dissolved in 10ml of chloroform then added in a reaction vessel (R) which is clamped in a thermostat at constant 298K temperature (as illustrated in the fig. (1)) after thermal equilibrium has been reached, bromine (Br_2) 10.77ml (0.015mol, 1.392mol dm^{-3}) added which is also allowed in 298K thermostat to come to temperature equilibrium before use. A pure nitrogen gas with constant speed 10 dm^3/hr. by using gas flow meter was passed through a reaction mixture (R) that can transfer the hydrogen bromide (HBr) gas which is formed from the reaction, to the three necked flask (A) which contains (200ml) distilled water at 298K, and the conductivity cell was fitted with a rubber stopper and the conductivity readings from conductivity meter (C) were recorded (the conductivity of distilled water as a blank was excluded). The other neck of the flask (A) connected by a rubber tube to the flask (I) which contains 10ml distilled water and indicator, the color dose not changed indicating that all HBr gas are trapped and dissolved in the flask (A) insuring the accuracy of the conductivity measurement. The experiment was repeated with the same weight and volumes of reactant at each (273, 283, 293, 303, 318)K, temperature, also for other sultams B and C.

2.3.2 Molar ratio (15:1) (Sultam A : Br_2)

Using concentrations by dissolving 3.5295g (0.015mol, 1.4923mol dm^{-3}) of 1,2-thiazine (Sultam A) 10ml of chloroform at 298K and the brominated agent, (Br_2) 0.0513ml (0.001mol, 0.0994mol dm^{-3}) was added.

2.3.3 Molar ratio (1:1) (Sultam A : Br_2)

Using concentrations by dissolving 0.235g (0.001mol, 0.197mol dm^{-3}) of 1,2-thiazine (Sultam A) 10ml of chloroform at 298K and the brominated agent, (Br_2) 0.0512ml (0.001mol, 0.1974mol dm^{-3}) was added.

III. RESULTS AND DISCUSSION

3.1 The bromination using sultam:Br_2 (1:15) molar ratio

The ability of conducting of the ions of hydrogen bromide (HBr) produced as a side product has been obtained by conductometric measurements, at six different temperatures (between 273- 318K). The conductivity of HBr were increased with time at constant temperature as shown in fig.(2) indicating as the temperature increased the amount of molecular interactions will increase as a result the reaction more quickly goes to the product. 2):Variation of conductivity of the HBr with time for bromination of sultams (A, B, C) at different temperature.

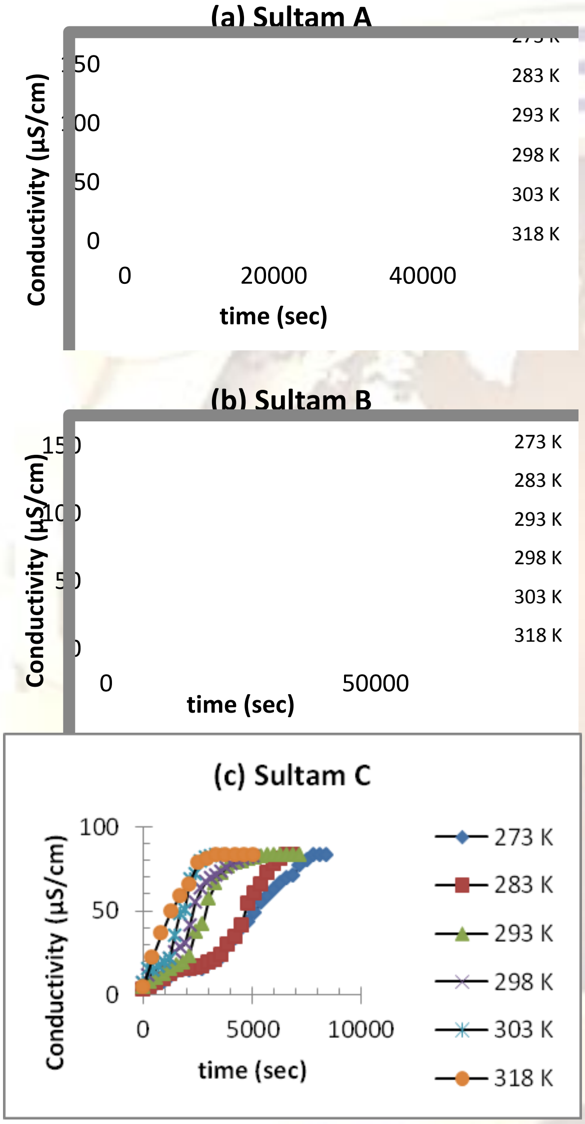


Figure (2):Variation of conductivity of the HBr with time for bromination of sultams (A, B, C) at different temperature.

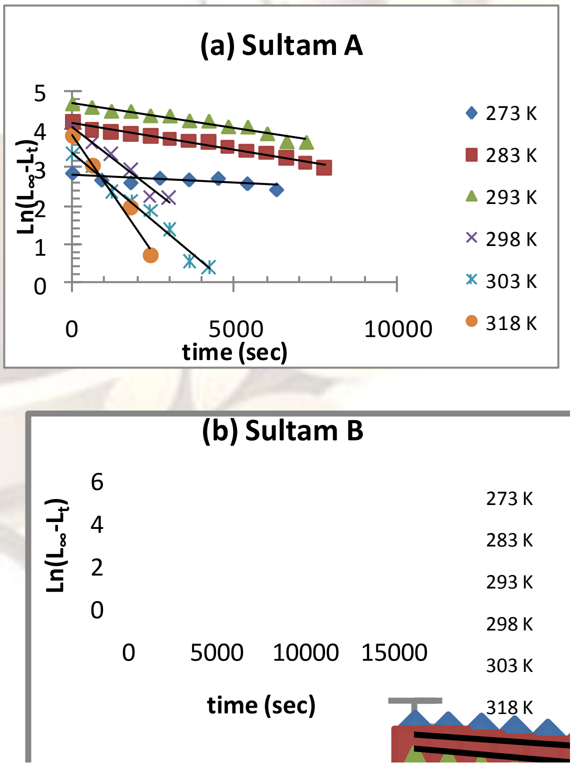
3.1.1 Interpretation of the overall kinetic and thermodynamic results

The results obtained from the kinetic data for the product of the bromination of sultams were found to follow pseudo first-order kinetics according to the equation (1). The rate constant values (k) at different temperature were calculated for the product from the pseudo first order equation[14,15]:

$$Ln(L_\infty - L_t) = \ln L_\infty - kt \qquad (1)$$

Where L_t: conductivity of the dissolved HBr gas at any time (t). L_∞: conductivity of the dissolved HBr gas at infinite time (t_∞). t: time in sec. k: rate constant of reaction in sec^{-1}. (L_∞-L_t): concentration of product at any time. The value of k for each temperature was evaluated from the slope of the linear plots of ln(L_∞-L_t) against (t), the data plots are shown in the fig. (3) and the summary of findings of k, $t_{1/2}$, and R^2 are given in the table(2), where $t_{1/2}$ is the half-life of the reaction R^2 is the correlation coefficient which is a measure of the goodness-of-fit of the regression and $0 \le R^2 \le 1$.

Pseudo first order equation was fitted for the data, since linear plots are formed as in the fig.(3) and R^2 correlation coefficient are given in table (2) which are very close to unity indicating excellent fit to the equation. Rate constant values and half time ($t_{1/2}$) value are shown in table (2). The k-value of (p-Cl)substituted sultam (B) which has electron withdrawing effect, rate constant decreased (k= 2×10^{-4} sec^{-1} at 298K) and $t_{1/2}$ increased ($t_{1/2}$ = 3465 sec), While for (p-OCH_3) substituted sultam (C) which increases the electron density at the reaction center, the k-value increased (k= 26×10^{-4} sec^{-1} at 298K) and $t_{1/2}$ decreased ($t_{1/2}$= 1952.3 sec.), as a result the same sequence of k-values that is obtained p-OCH_3 > H > p-Cl.



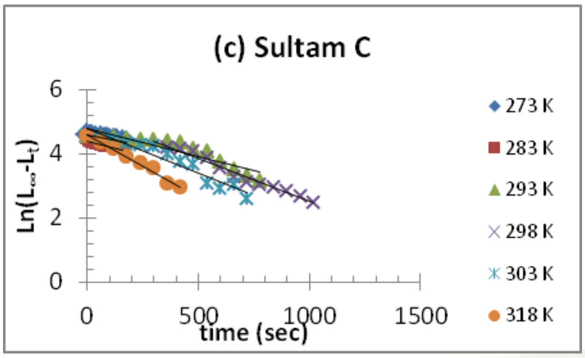


Figure (3): pseudo first order plot for the conductivity of the HBr of sultam (A, B, C) with bromine in chloroform using 1:15 molar ratio reactants.

Table (2): Observed rate constants, for the bromination of sultams by Br_2 with molar ratio (1:15).

(a) For sultam A

Temp.(K)	**$k_{obs}\times10^{4}(sec^{-1})$**	**$t_{1/2}$ (sec)**	**R^2**
273	0.72	9625	0.960
283	1.5	4620	0.982
293	3	2310	0.962
298	4	1732.5	0.969
303	9	770	0.921
318	16	433.125	0.974

(b) For sultam B

Temp.(K)	**$k_{obs}\times10^{4}(sec^{-1})$**	**$t_{1/2}$ (sec)**	**R^2**
273	0.3	23100	0.974
283	0.7	9900	0.984
293	1.4	4950	0.997
298	2	3465	0.956
303	4	1732.5	0.951
318	10	693	0.943

(c) For sultam C

Temp. (K)	**$k_{obs}\times10^{-4}(sec^{-1})$**	**$t_{1/2}$ (sec)**	**R^2**
273	9.8	5179.7	0.979
283	16	3172.589	0.906
293	21	2417.211	0.945
298	26	1952.3	0.972
303	31	1637.465	0.913
318	52	976.1	0.984

The rate constants for the reaction at the six different temperatures were plotted against 1/T and the activation energy (E_a) was calculated from the slope of the Arrhenius plot (as shown in fig. (6)) which shows a good straight line with the slope of ($-E_a/R$) as in the equation (2):

$$\ln k = \ln A - E_a / RT \qquad (2)$$

From the obtained results of the activation energy E_a, the enthalpy of activation $\Delta H^{\#}$, entropy $\Delta S^{\#}$ and Gibbs free energy of activation $\Delta G^{\#}$ can be obtained using equations[11,13]:

$$\Delta H^{\#} = E_a - RT \qquad (3)$$

$$A = \frac{eKT}{h} e^{\frac{\Delta S^{\#}}{R}} \qquad (4)$$

$$\Delta S^{\#} = R(LnA - Ln(ek_b T / h)) \qquad (5)$$

$$\Delta G^{\#} = \Delta H^{\#} - T\Delta S^{\#} \qquad (6)$$

where $k_b = 1.3806*10^{-23}$ J K^{-1}, $h = 6.626*10^{-34}$ J sec.

Table(3) show that the reactants needs higher energy to reach transition state for the sultam (B) (E_a = 56.797 KJ. mol^{-1}) as compared with unsubstituted sultam (E_a= 51.586 KJ.mol^{-1}) while lower energy needed for sultam (C) (E_a = 19.579 KJ.mol^{-1}) this is due to electron withdrawing and donating effect respectively. $\Delta H^{\#}$ values are positive (as in table (4)) indicating the endothermic behavior for these reactions.

The values of $\Delta H^{\#}$ are positive means consumes energy in its process. Relatively low values of (A) pre-exponential factor were explained according to the transition state theory[12], by the decrease in partition function of the transition state, Q^{*}_{AB}, and the increase in the partition functions of the reactants, Q_A and Q_B, according to the equation (7):

$$A = \frac{KT}{h} * \frac{Q^{*}_{AB}}{Q_A Q_B} \qquad (7)$$

Which indicate the more rigid configuration with less degrees of freedom for the activated complex which has a simpler configuration than the reactant molecules. The study of the bromination of sultams are gave negative low values for $\Delta S^{\#}$ as shown in table (3,4), $\Delta S^{\#}$ value for (p-Cl) substituted sultam (B) ($\Delta S^{\#}$= -132.209 J $K^{-1}mol^{-1}$) electron withdrawing group causes unstable transition state, while for (p-OCH_3) substituted group($\Delta S^{\#}$= -237.448 $JK^{-1}mol^{-1}$) which formed more stable transition state.

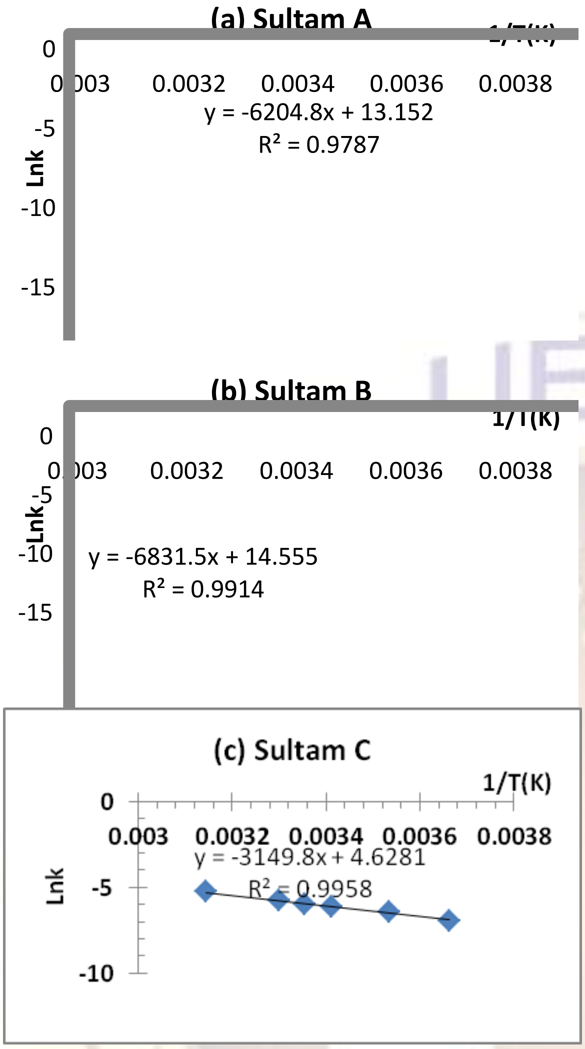


Figure (4): Arrhenius plots for bromination of sultams (A, B, C) at different temperatures using (1:15) molar ratio of sultam: Br_2.

Table (3): Arrhenius parameters and entropies of activation for the bromination of sultams (A, B, C) using (1:15) molar ratio of sultam: Br_2.

Sultam	E_a (KJ.mol^{-1})	R^2	A-factor/ s^{-1}	$\Delta S^{\#}$ (J K^{-1}mol^{-1}) at 298K
A	51.586	0.978	5.150×10^5	-143.874
B	56.797	0.991	2.094×10^6	-132.209
C	26.187	0.986	1.023×10^2	-214.742

Table (4): Thermodynamic parameters for the bromination reaction of sultams (A, B, C) using (1:15) molar ratio of sultam: Br_2.

Sultam	Temp. (K)	$\Delta H^{\#}$(KJ.mol^{-1})	$\Delta S^{\#}$ (JK^{-1}mol^{-1})
A	273	49.316	-143.145
	283	49.233	-143.444
	293	49.150	-143.733
	298	49.109	-143.874
	303	49.067	-144.012
	318	48.942	-144.414
B	273	54.527	-131.481
	283	54.444	-131.780
	293	54.361	-132.068
	298	54.319	-132.209
	303	54.277	-132.347
	318	54.153	-132.749
C	273	23.917	-214.014
	283	23.834	-214.313
	293	23.751	-214.602
	298	23.709	-214.742
	303	23.668	-214.881
	318	23.543	-215.282

3.2 The bromination using sultam : Br_2 (15:1) molar ratio

For Sultam:Br_2 (15:1) reaction, H^1- and C^{13}-nmr, IR and UV-data are very close to un substituted sultam. Of course a reaction has been achieved between 1mmole of bromine and 15mmole sultam but the product disappeared between the large quantities of sultam.

3.3 The bromination using sultam : Br_2 (1:1) molar ratio

The study of bromination of sultams also carried out using equi molar ratio of each reactants (sultam and Br_2), the variation of conductivity with time are shown in fig.(5) as we see the conductivity of the HBr increase with time indicating that the reactions are clean forward processes, since no equilibrium was observed during kinetic runs.
The rate law can be expressed by the equation:

$$\frac{d[product]}{dt} = k[Br_2][Sultam] \qquad (8)$$

These reactions were determined as second order equation; first-order with respect to each reactant and can be described by equation (9)[14-17].

$$\frac{L_t}{L_\infty(L_\infty - L_t)} = kt \qquad (9)$$

Which means that the straight line plot of $L_t/(L_\infty(L_\infty - L_t))$ with the time (t) has a slope (k) which is the second order rate constant, the plots show excellent fit to the second order equation as shown in fig. (6) and the data are tabulated in the table (5).

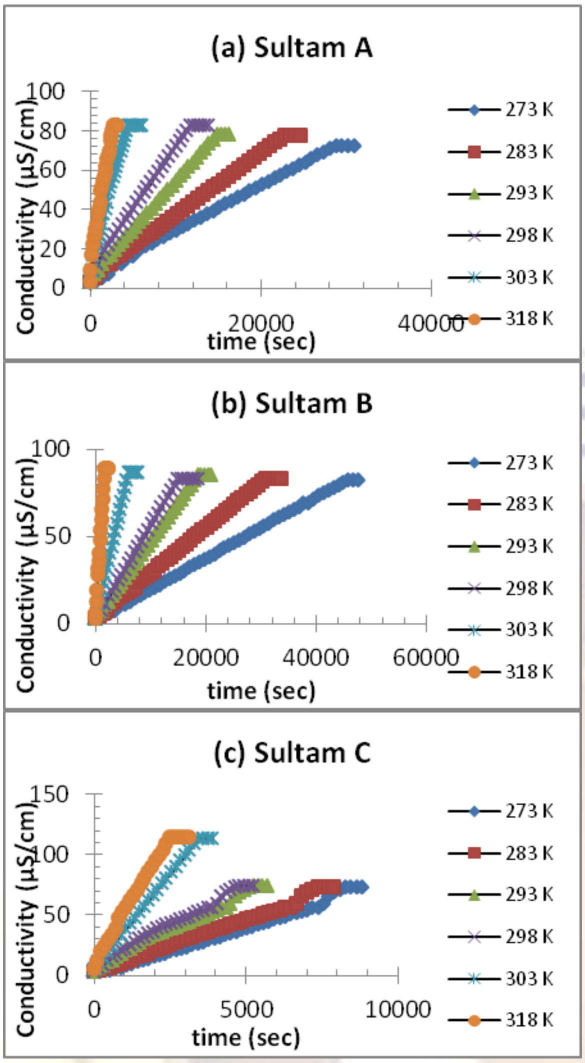
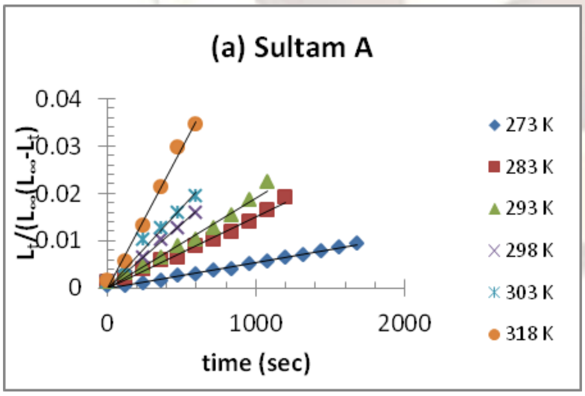


Figure (5): Variation of conductivity of HBr with time for bromination of sultams (A, B, C) at different temperatures using (1:1) molar ratio of sultam: Br_2.



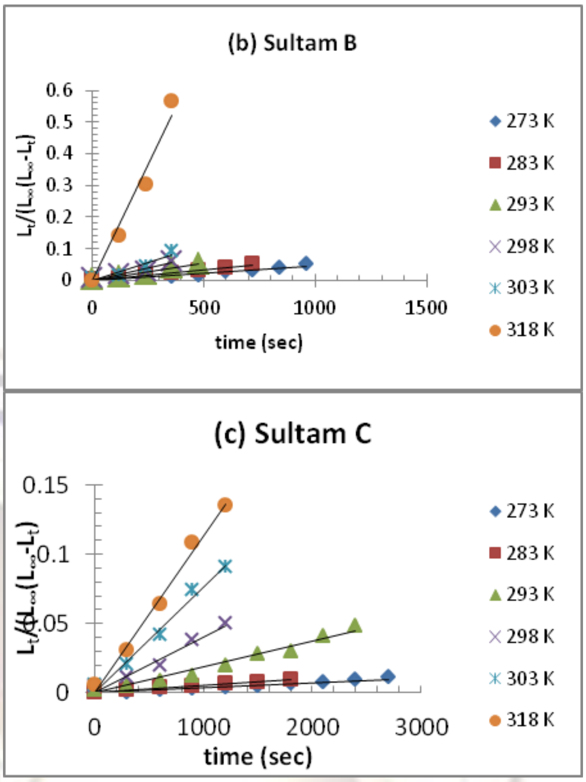


Figure (6): second order plot for the conductivity of HBr for bromination of sultams (A, B, C) at different temperatures using (1:1) molar ratio of sultam: Br_2.

Due to electron withdrawing effect of (p-Cl)substituted sultam (B) in table (5) k-values are smaller as compared with unsubstituted sultam (A) indicates that the reaction are slower which is decreases the electron density at the reaction center, while the k-values are higher in the presence of (p-OCH_3) which is electron donating group which is increase the electron density on the reaction center.

Table (5): Observed rate constants, for the bromination of sultams with Br_2.

(a) For sultam A
(b) For sultam B

Temp. (K)	$k_{obs}\times10^{-4}$ ($sec^{-1}.L.mol^{-1}$)	$t_{1/2}$ (sec)	R^2
273	1.9	26716.54	0.960
283	5	10152.28	0.944
293	12	4230.118	0.937
298	18	2820.079	0.929
303	27	1880.053	0.917
318	88	576.8343	0.914

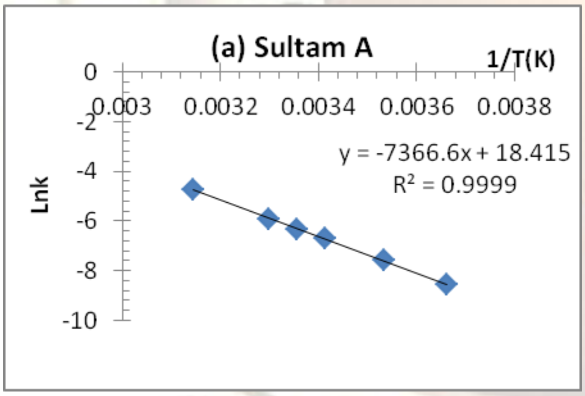
Temp. (K)	$k_{obs}\times10^{-4}$ ($sec^{-1}.L.mol^{-1}$)	$t_{1/2}$ (sec)	R^2
273	1	50761.42	0.963
283	3.4	14929.83	0.937
293	10	5076.142	0.958
298	16	3172.589	0.904
303	27	1880.053	0.984
318	61	437.5985	0.908

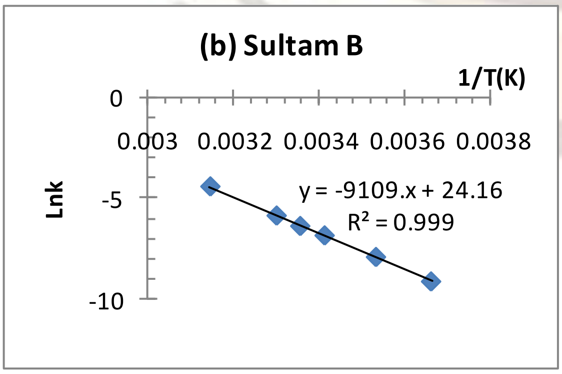
(c) For sultam C

Temp. (K)	**$k_{obs}\times10^{-4}$ ($sec^{-1}.L.mol^{-1}$)**	**$t_{1/2}$ (sec)**	**R^2**
273	11	4614.675	0.991
283	16	3172.589	0.935
293	23	2207.018	0.996
298	27	1880.053	0.986
303	31	1637.465	0.906
318	49	1035.947	0.963

3.3.1 Interpretation of the overall kinetic and thermodynamic results

Also the electronic (withdrawing and donating) effect are seen in the activation energies as in table (6), the sequence of E_a is : p-Cl > H > p-OCH_3. The reactions are consumes energy in its processes, they are endothermic reactions giving positive values of $\Delta H^{\#}$. The abnormal value of (A) pre-exponential value and low negative value of $\Delta S^{\#}$ indicates the more rigid configuration with less degrees of freedom for the activated complex than those of the reactant molecules, also the presence of electron withdrawing effect (p-Cl) lead to higher value of $\Delta S^{\#}$ ($\Delta S^{\#}$= 52.287 $JK^{-1}mol^{-1}$ at 298K) comparing with unsubstituted sultam ($\Delta S^{\#}$= -100.117 $JK^{-1}mol^{-1}$ at 298K) which causes unstable transition state, but the presence of the electron donating group lead to lower value of $\Delta S^{\#}$ ($\Delta S^{\#}$= -222.190 $JK^{-1}mol^{-1}$ at 298K)
which produces the more stable transition state.





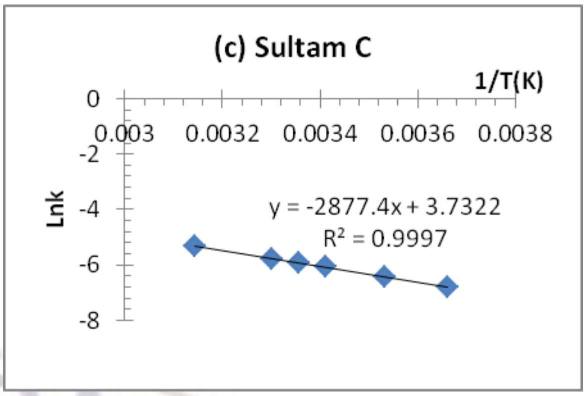


Figure (7): Arrhenius plots for bromination of sultams (A, B, C) at different temperatures using (1:1) molar ratio of sultam: Br_2.

Table (6): Arrhenius parameters and entropies of activation for the bromination of sultams (A, B, C) using (1:1) molar ratio of sultam: Br_2.

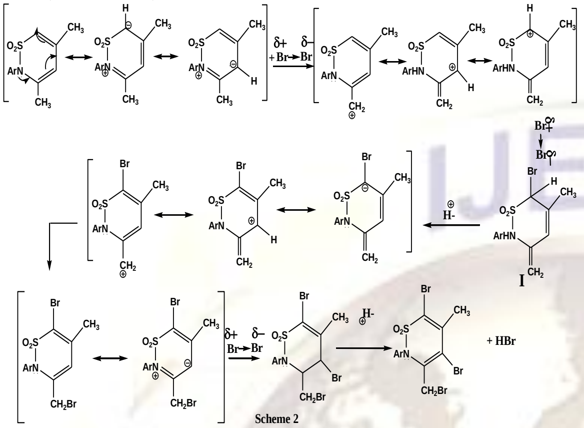
Sultam	E_a ($KJ.mol^{-1}$)	R^2	A-factor ($sec^{-1}.L.mol^{-1}$)	$\Delta S^{\#}$ ($J K^{-1}mol^{-1}$) at 298K
A	61.245	0.999	9.943×10^{7}	-100.117
B	75.733	0.999	3.133×10^{10}	-52.287
C	23.922	0.999	0.239×10^{2}	-222.190

Table (7): Thermodynamic parameters for the bromination reaction of sultams (A, B, C) using (1:1) molar ratio of sultam: Br_2.

Sultam	Temp. (K)	$\Delta H^{\#}$ ($KJ.mol^{-1}$)	$\Delta S^{\#}$ ($J K^{-1}mol^{-1}$)
A	273	58.976	-99.3890
	283	58.893	-99.6881
	293	58.809	-99.9768
	298	58.768	-100.117
	303	58.726	-100.255
	318	58.602	-100.657
B	273	73.463	-51.558
	283	73.380	-51.857
	293	73.297	-52.146
	298	73.255	-52.287
	303	73.213	-52.425
	318	73.089	-52.827
C	273	21.652	-221.461
	283	21.569	-221.760
	293	21.486	-222.049
	298	21.445	-222.190
	303	21.403	-222.328
	318	21.278	-222.730

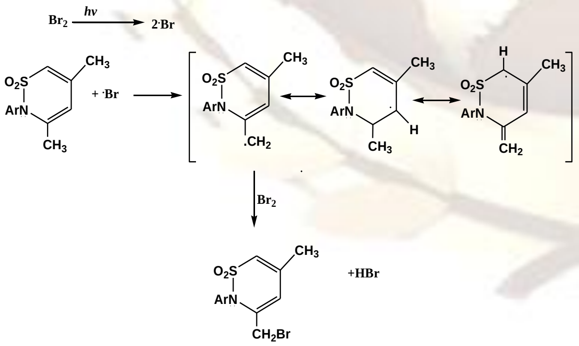
3.4 Reaction mechanism

With the assumption that 1,2-thazine nuclei are nucleophilic, and with the sure knowledge that alkene linkages are present in such nuclei, it is reasonable to picture at least the initial stages of aromatic substitution as being exactly analogous to the typical nucleophilic additive reactions. Hence the accepted mechanism for the reaction was(scheme 2)[18]:



Scheme 2

The most easier mechanism was expected for bromination of 1,2-thiazine is electrophilic aromatic reaction, under the influence of the attacking bromine molecule, the 1,2-thiazine molecule is polarized as indicated, and the negative carbon(nucleophile) attacks positively polarized bromine to produce structure (I) the easier reaction is possible; is that the intermediate structure (I) may lose a proton by the negative charged bromine to produce HBr. Under more vigorous reaction conditions, and with more bromine, with the presence of alkyl group which activate an aromatic nucleus toward electrophilic substitution; hence toluene is brominated more readily than is benzene. But the most proposed mechanism which can be passed through free radical substitution reaction(scheme 3):



Scheme (3)

IV. CONCLUSION

The proposed experimental techniques that have been used in kinetics and thermodynamic studies are quite simple and free from rigid experimental conditions and are characterized by wide linear dynamic ranges and high sensitivity.

The importance of the present investigation is to demonstrate the possibility of using a modern conductometer to investigate these reaction kinetics.

ACKNOWLEDGEMENTS

My deepest appreciation and gratitude to the higher education council, Salahaddin university-Erbil.

REFERENCES

[1] Hansch C.; Sammes P.G., Comprehensive Medicinal Chemistry, Pergamum press, Oxford, 1990.

[2] Hanson P. R.; Probst D. A.; Robinson R. E.; Yau M., Tetrahedron let., 1999,40, 4761.

[3] Seyden P.J. Chiral Auxiliaries and Ligands in Asymmetric synthesis, Wiley, New York, 1995.

[4] Brown R.C.; Castro J.L.; Moriggi J-D, Tetrahedron Let. 2000, 41, 3681.

[5] Jenkins A., IUPAC compendium of chemical Terminology, 2nd Ed. 67, 1370, 1995.

[6] Burckhardt H.; Bonner T.; Bonu, Germany, U.S. Pattent. No. 2,917,512, Dec.15, 1959.

[7] Hans F.; Beeck D.; Tummes H.; Duisburg-Meiderich, Germany, U.S. pattent. No. 2,866,786, Dec. 30, 1958.

[8] Braim R.R.; Ketuly K.A.; Hadi A.H.; Khaledi H. Acta Crystaaographic o2775, E67, 2011.

[9] Fanghenel E.; Mohammed H.; Richter A.M.; Radeglia R.; J. Pract. Chem., 1984 326, 545.

[10] Fanghanel E., Muhammed H.A. Keta Y., J. Pract. Chem., 1982, 324.

[11] Gowenlock B.G., Quart. Rev., 1960, 140, 133.

[12] Missen R.W.; Mims Ch. A.; Saville B. A., Introduction to chemical reaction engineering and kinetics, 1998.

[13] Barrow G.M., Physical chemistry (McGrow Hill Inc), 4th Ed., 1979.

[14] Hill Ch. G., An introduction to chemical engineering kinetics and reactor design John Wiley and Sons New York, 1977.

[15] Atkins P.W. Physical chemistry, Oxford University Press, USA 5th Ed., 1995.

[16] Laidler K.J., A glossary of terms used in chemical kinetics, including reaction dynamics Pure & Applied Chemistry, 68, (1), 1996, 149-192.

[17] Alberty S.; Robert J.; Robert A., Physical chemistry (John Wiley and sons, Inc. New York, 3rd edition, 2001).

[18] Royals E.E., Advanced organic chemistry (prentice Hall United States America, 1961).