

SYNTHESIS, REACTION MECHANISM AND KINETIC STUDY OF 5-CHLORO, 2-METHYL ANILINE PHOSPHATE DI-ESTER IN ACID MEDIA

Dr. Amit chaudhary Chem. Dept., D.S. College, Aligarh

Email- amitchaudhary111114@gmail.com

ABSTRACT- Kinetic measurement of the hydrolysis of di-5-chloro, 2-methyl aniline phosphate ester has been carried out in the acid range 0.1 to 6.0 mol. dm⁻³ HCl at 80 ± 0.5 °C in 20% aqueous dioxane mixture. The inorganic phosphate obtained in overall hydrolysis has been estimated colorimetrically by Allen's modified method [1]. The overall systematic ionic data proves the presence of acid catalysed hydrolysis. In the hydrolysis of diester conjugate acid, neutral and mononegative species have been found to be reactive, but in this discussion only conjugate acid species have been given. The first order rate coefficients have been calculated using integrated form of the corresponding rate equation.

$$K_e = K_H^+ \cdot C_H^+ \cdot \exp. \mu$$

The rate coefficients estimated by the above equation are fairly in good agreement with experimentally observed rate. Arrhenius parameters, Linear free energy relationship etc. have been used to propose probable mechanism. Temperature, solvent, substrate concentration effects etc. have been studied to find out the participation of water molecule, bond-fission and molecularity of the reaction.

INTRODUCTION: The recent interest in biochemistry of di-ester [2, 3] having C-N-P linkage [4 - 21], reflects the current emphasis on acid hydrolysis of 5-chloro, 2-methyl aniline phosphate di-ester. In this field chemical research has entered into a new dimension leading to the synthesis of organophosphate pesticides [22 - 24], insecticides [25 - 26] and plant hormones [27] etc. Bunton and co-workers [28] found that acid catalysed hydrolysis occurs only when an electron attracting substituent is present in aryl part.

EXPERIMENTATION : The method of preparation of the phosphate di-ester of 5-chloro, 2-methyl aniline has been done by general methods [29 - 30] which involves the direct reaction of POCl₃ with respective amine. The residue left after removing 5-chloro, 2-methyl aniline phosphate mono-ester was washed with hot distilled water and 0.5 mol. dm⁻³ NaOH solution was added to remove 5-chloro, 2-methyl aniline phosphate monoester and unreacted POCl₃. The aryl amine finally digested in 5.0 mol dm⁻³ NaOH to separate di-ester from tri-ester. It was filtered off and the filtrate was acidified with dilute HCl using phenolphthalein as an indicator. The white precipitate so obtained was separated by filtration and made free from hydroxyl ions with repeated washings with hot distilled water. It was then dried at room temperature and recrystallised with absolute ethyl alcohol to give a white crystalline solid, which was identified as 5-chloro, 2-methyl aniline phosphate diester with following physical properties:

1. **Melting point (observed) = 266°C**
2. **Theoretical Percentage of 'P' = 8.93**
Observed percentage of 'P' = 8.72
3. **Infra Red spectrum (fig.1) of diester showed the appearance of absorption bands characteristics of**
adjacent H = 820,800 cm^{-1} .
aromatic ring = 940 cm^{-1} .
O
||
P — OH = 988 cm^{-1} .
P — OH = 1122 cm^{-1} .
Secondary amine = 1230 cm^{-1}
P = N = 1422 cm^{-1} .
tri substituted = 1500 cm^{-1} .
Aromatic ester = 1738 cm^{-1} .

All the above properties confirm the structure of di- 5-chloro, 2-methyl aniline phoshate ester.

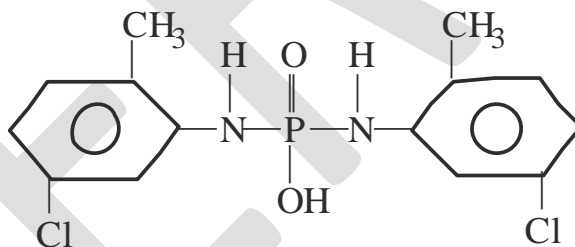
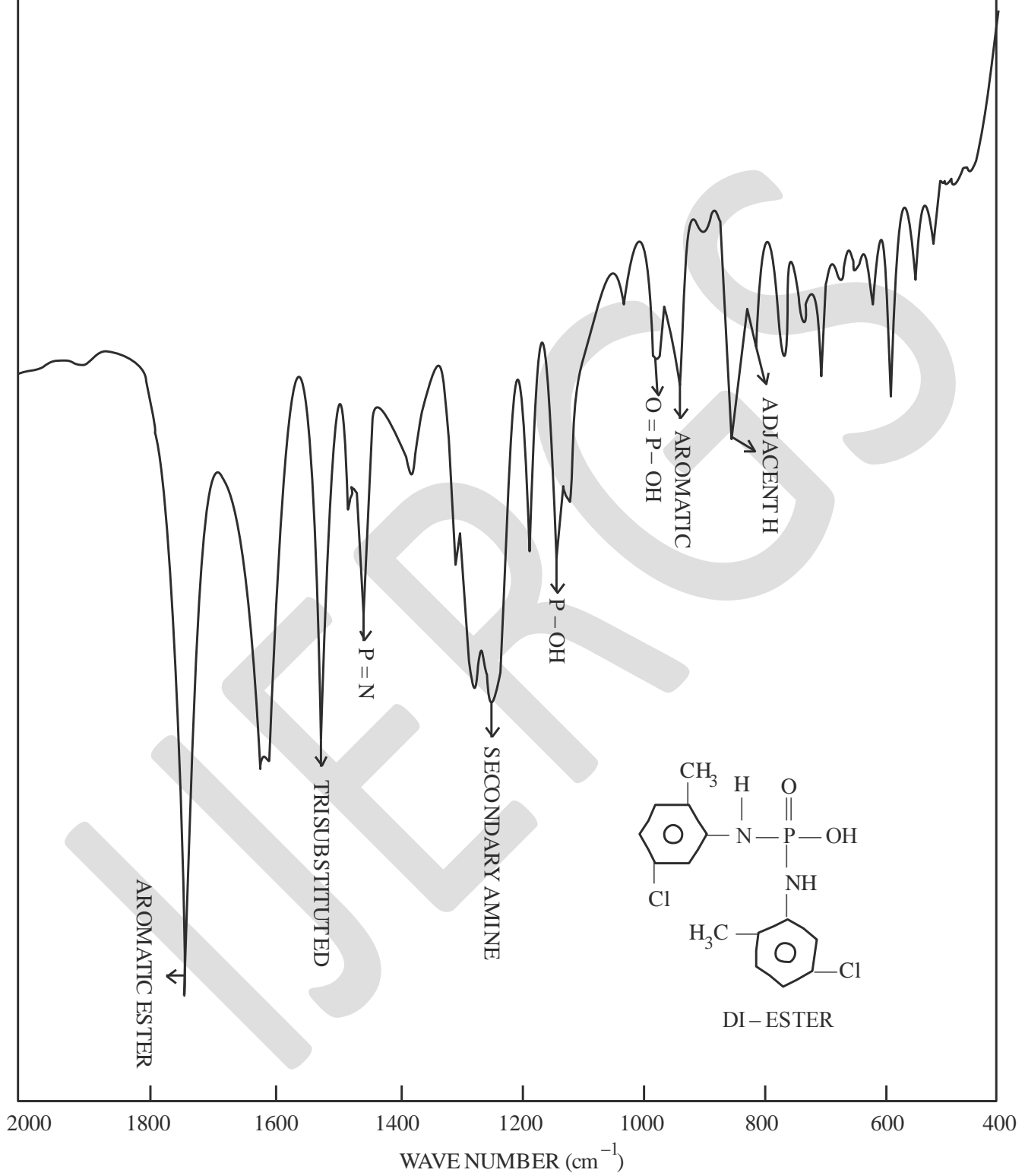


FIG. 1. IR SPECTRUM FOR 5-CHLORO, 2-METHYL ANILINE PHOSPHATE DIESTER.



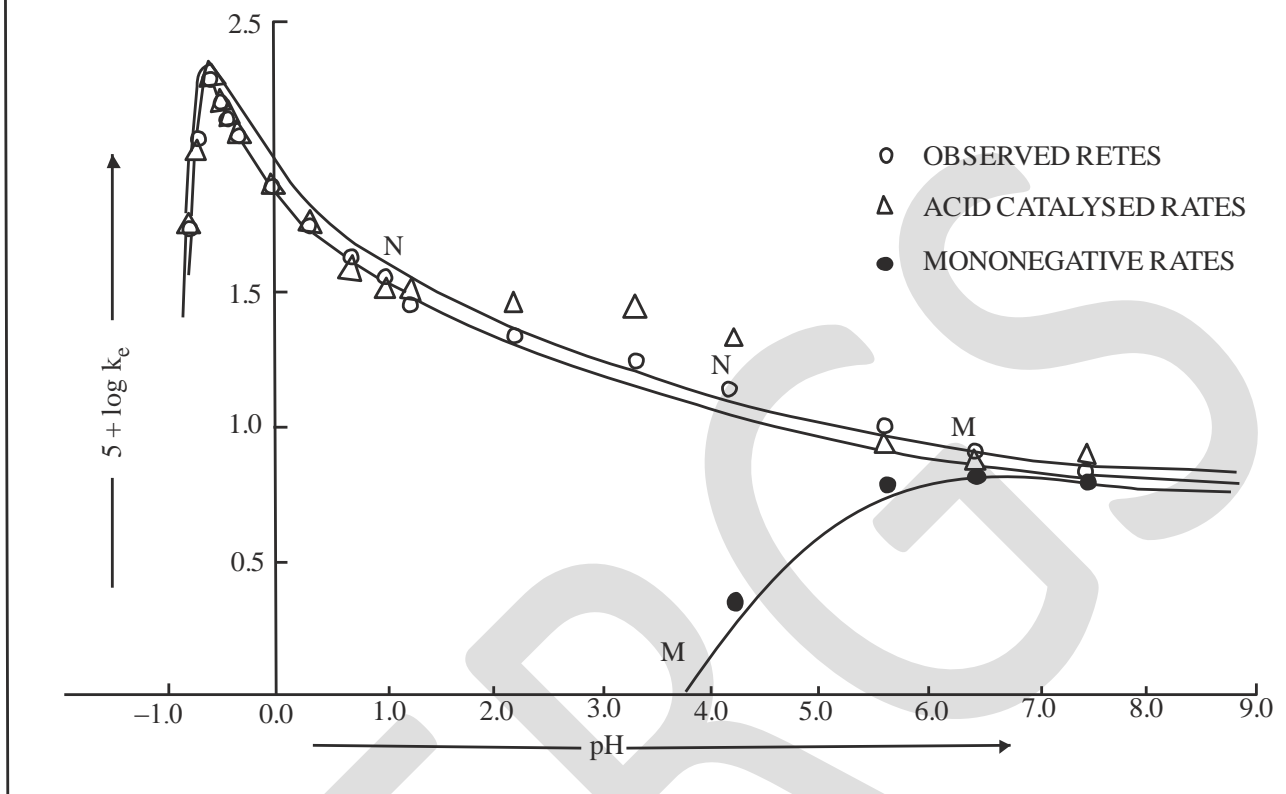
RESULT AND DISCUSSION :

HYDROLYSIS VIA CONJUGATE ACID SPECIES : The investigation of the hydrolysis of di- 5-chloro, 2-methyl aniline phosphate ester shows that it is reactive via neutral, mono-negative and conjugate acid species. The kinetic study of the hydrolysis of above diester have been carried in acid and buffer media in the region 0.1 to 6.0 mol dm⁻³ and pH 1.24 to 7.46 at a temperature 80 ± 0.5°C. Kinetic runs were made in 20% aqueous dixon due to its solubility reasons. Table I and Fig II summarises the pseudo first order rate coefficient of the hydrolysis of 5-chloro, 2-methyl aniline phosphate diester.

TABLE 1. pH log RATE PROFILE OF DI-5-CHLORO, 2-METHYL ANILINE PHOSPHATE AT 80 ± 0.5°C

HCl (mol dm ⁻³)	pH	10 ⁵ ke.(mol dm ⁻³ min ⁻¹) (obsd.)	5 + log ke.
6.0	-0.778	58.24	1.74
5.0	-0.699	112.60	2.05
4.0	-0.602	197.66	2.29
3.0	-0.477	165.31	2.21
2.5	-0.400	146.29	2.16
2.0	-0.300	126.44	2.10
1.0	0.000	80.32	1.90
0.5	0.301	56.30	1.75
0.2	0.700	43.12	1.63
0.1	1.000	35.78	1.55
Buffers-			
Composition of buffers have been given in experimental section	1.24	29.16	1.46
	2.20	21.85	1.34
	3.30	17.37	1.24
	4.17	13.48	1.13
	5.60	9.77	0.99
	6.43	7.94	0.90
	7.46	6.76	0.83

FIG.II pH – log RATE PROFILE OF DI – 5 – CHLORO, 2 – METHYL ANILINE PHOSPHATE AT 80°C



Result shows that the rate increases with the increase in acid medium upto $4.0 \text{ mol dm}^{-3} \text{ HCl}$. Further rise in acidity bring about lowering in rates. This bend in pH log rate profile could be determined by carrying out kinetic runs at constant ionic strength. The cause of bend may be due to water activity effect or ionic strength effect or due to simultaneous action of both.

EFFECT OF IONIC STRENGTH :

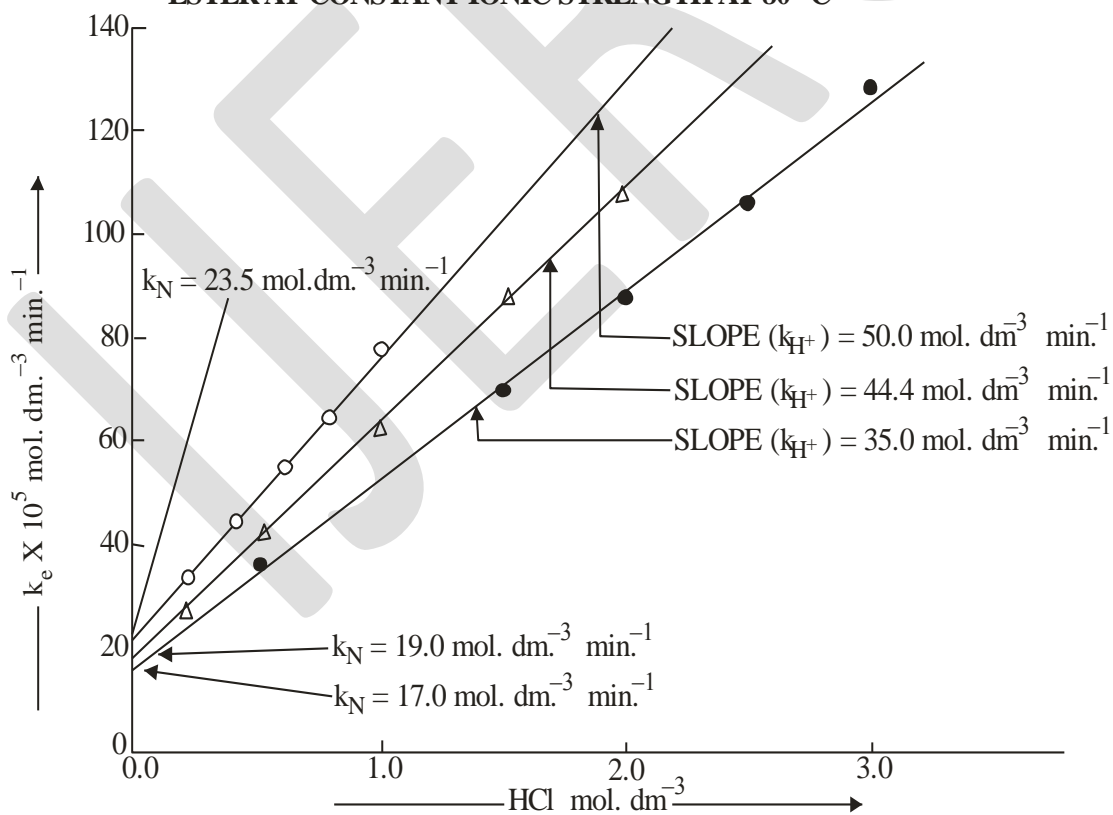
The ionic strength effect on the rate of hydrolysis of 5-chloro, 2-methyl aniline phosphate diester was examined by carrying out kinetic runs at different ionic strength by using appropriate mixture of KCl and HCl acid. Table-2 summarises the rate coefficient and Fig III describes a plot of log rate Vs acid molarities, which gives three linear curves indicating the presence of acid catalysis. Different intercepts on the rate axis are the neutral rate at corresponding ionic strength.

TABLE 2. HYDROLYSIS OF DL-5-CHLORO, 2-METHYL ANILINE PHOSPHATE AT CONSTANT IONIC STRENGTH AT 80°C

Ionic Strength (μ)	Composition		$10^5 k_e$ ($\text{mol dm}^{-3} \text{ min}^{-1}$) (obsd.)
	HCl (mol dm^{-3})	KCl (mol dm^{-3})	
1.0	0.2	0.8	34.01
1.0	0.4	0.6	44.72
1.0	0.6	0.4	55.00
1.0	0.8	0.2	63.04
1.0	1.0	0.0	77.56
2.0	0.2	1.8	27.20
2.0	0.5	1.5	43.13
2.0	1.0	1.0	61.72
2.0	1.5	0.5	88.43
2.0	1.8	0.2	98.63
2.0	2.0	0.0	108.10
3.0	0.5	2.5	36.11
3.0	1.5	1.5	70.10
3.0	2.0	1.0	87.63
3.0	2.5	0.5	106.72
3.0	3.0	0.0	129.00

FIG. III

HYDROLYSIS OF DI - 5 - CHLORO, 2 - METHYL ANILINE PHOSPHATE ESTER AT CONSTANT IONIC STRENGTH AT 80° C



Variation of the neutral rates with ionic strength is governed by the following rate expressions.

$$K_H^+ = K_{H_0}^+ \exp b_H^+ \cdot \mu \quad (1)$$

or,
$$K_H^+ \cdot C_H^+ = K_{H_0}^+ \cdot C_H^+ \exp. b_H^+ \cdot \mu \quad (2)$$

or,
$$5 + \log K_H^+ \cdot C_H^+ = 5 + \log K_{H_0}^+ + \log C_H^+ + b'_H \cdot \mu \quad (3)$$

where K_H^+ , $K_{H_0}^+$, b'_H and μ are specified acid catalysed rates at that ionic strength, at zero ionic strength and ion strength respectively

Similarly, the specific neutral rates may be represented as follows :

$$K_N = K_{N_0} \exp b_N \cdot \mu \quad (4)$$

or,
$$5 + \log K_N = 5 + \log K_{N_0} + b'_N \cdot \mu \quad (5)$$

where K_N , K_{N_0} , b'_N and μ are specific neutral rates at that ionic strength, at zero ionic strength, a constant and ionic strength

respectively where b'_H and $b'_N = \frac{b}{2.303}$.

The equation (3) and (5) may be used to compute the acid catalysed and neutral rates at each experimental molarity. Thus both acid catalysed and neutral rates may be represented as :

$$K_e = k_H^+ \cdot C_H^+ + K_N \quad (6)$$

The specific acid catalysed and specific neutral rates for the hydrolysis of diester which have been calculated from the above equations have summarised in table 3.

TABLE 3. SPECIFIC ACID CATALYSED [K_H^+] AND SPECIFIC NEUTRAL [K_N] RATES FOR THE HYDROLYSIS OF 5-CHLORO, 2-METHYL PHOSPHATE DIESTER AT DIFFERENT IONIC STRENGTH AT 80°C.

Ionic Strength (μ)	$10^5 K_H^+$ ($\text{mol dm}^{-3} \text{ min}^{-1}$)	$5 + \log K_H^+$	$10^5 K_N$ ($\text{mol dm}^{-3} \text{ min}^{-1}$)	$5 + \log K_N$
1.0	50.0	1.69	23.5	1.37
2.0	44.4	1.64	19.0	1.27
3.0	35.0	1.54	17.0	1.23

With the help of above equations, theoretical rates can be calculated which are then compared with the experimental rates and there is a remarkable similarities between the two rates upto 4.0 mol. dm^{-3} HCl. The value of acid catalysed ($5 + \log K_{H_0}^+ = 1.77$) and specific neutral rate ($5 + \log K_{N_0} = 1.46$) can be obtained from the intercepts on the rate axis while $b'_H = -0.031$ and $b'_N = -0.033$ can be obtained from the slopes of fig. IV

FIG. IV HYDROLYSIS OF DI - 5 - CHILORO, 2 - METHYL ANILINE PHOSPHATE AT 80° C (log SPECIFIC RATE Vs IONIC STRENGTH)

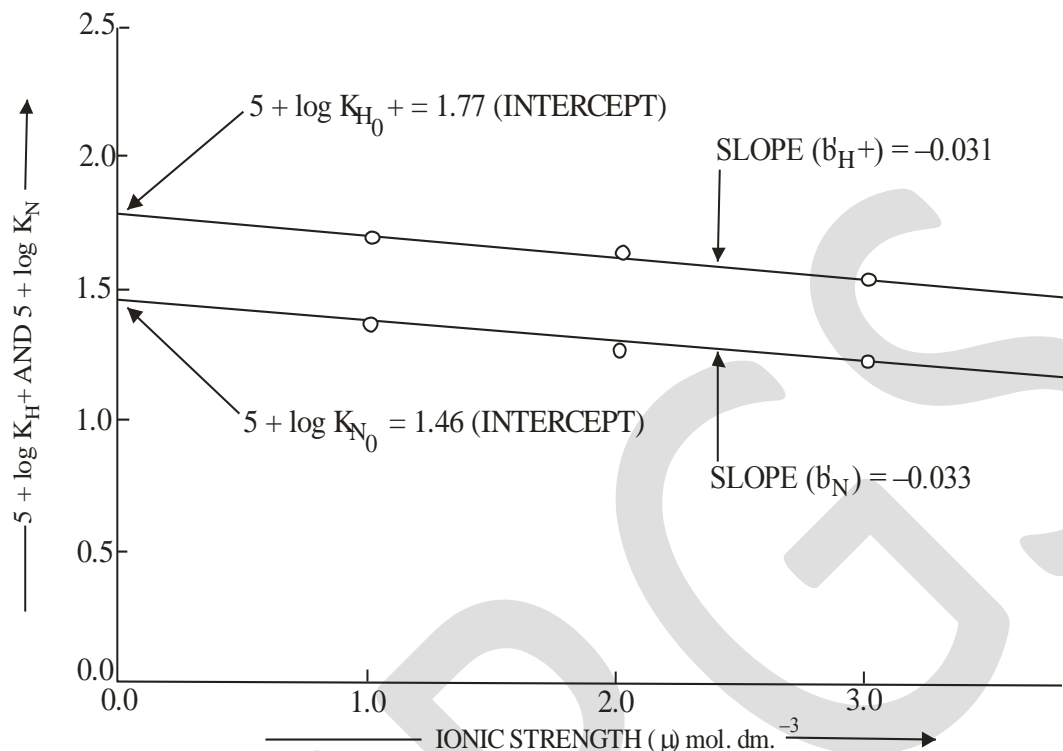


Table 4 summarises both the observed and calculated rates of hydrolysis of di-5-chloro, 2-methyl aniline phosphate at 80°C in the acid region from 1.0 to 6.0 mol dm⁻³ HCl. It is clear from the results that there is fairly good agreement between calculated and experimentally observed rates upto 4.0 mol dm⁻³ HCl. There is steep fall in the rates, beyond 4.0 mol dm⁻³ HCl which has been presumed due to participation of water molecule as a second reaction partner in the nucleophilic substitution reaction. Thus acid catalysed and neutral rates have been calculated by the modified form suggested by Bronsted-Bjerrum [31, 32]

$$K_{H^+} \cdot C_{H^+} = K_{H^+} \cdot \exp. b_{H^+} \cdot \mu (a_{H_2O})^n \quad (7)$$

and its logarithmic form can be showed as :

$$5 + \log K_{H^+} \cdot C_{H^+} = 5 + \log K_{H^+} + \log C_{H^+} + b'_{H^+} \cdot \mu + n \log a_{H_2O} \cdot \quad (8)$$

and neutral rates at higher concentration are as follows.

$$K_N = K_{N_0} \exp. b_N \cdot \mu (a_{H_2O})^n \quad (9)$$

and its logarithmic form can be showed as

$$5 + \log K_N = 5 + \log K_{N_0} + b'_N \cdot \mu + n \log a_{H_2O} \quad (10)$$

Where (a_{H₂O}) is water activity and n is an integer value.

TABLE 4 : CALCULATED AND OBSERVED RATES FOR THE HYDROLYSIS OF DI- 5-CHLORO, 2-METHYL ANILINE PHOSPHATE AT 80°C

HCl (mol. dm ⁻³)	10 ⁵ .K _N (mol.dm. ⁻³ min ⁻¹) from eq. (5)	10 ⁵ . K _{H⁺} + C _{H⁺} (mol. dm. min. ⁻¹) from eq. (3)	10 ⁵ . K _{H⁺} . C _{H⁺} (mol.dm ⁻¹) from eq. (8)	10 ⁵ . KN (mol.dm ⁻³ . Min. ⁻¹) from eq. (10)	Ke. 10 ⁵ (mol. dm. ⁻³ min. ⁻¹) (calcd.) from eq. (6)	5+log Ke (calcd.)	10 ⁵ . Ke (mol. dm ⁻³ min. ⁻¹) (obsd.)
0.1	28.62	5.84	–	–	34.46	1.53	35.78
0.2	28.40	11.58	–	–	39.98	1.60	43.12
0.5	27.76	28.47	–	–	56.23	1.75	56.30
1.0	26.73	54.82	–	–	81.55	1.91	80.32
2.0	24.77	101.85	–	–	126.62	2.10	126.44
2.5	23.85	123.73	–	–	147.58	2.16	146.29
3.0	22.96	142.56	–	–	165.52	2.21	165.31
4.0	21.28	177.01	–	–	198.29	2.29	197.60
5.0	19.72	206.06	100.92*	9.66*	110.58	2.04	112.60
6.0	18.28	258.22	53.57*	4.25*	57.82	1.76	58.24

Where, n = 0 for 0.1 to 4.0 mol dm⁻³ HCl and n* = 2, 3 respectively for 5.0 and 6.0 mol dm⁻³ HCl for acid and neutral rates Table 5 summarises Arrhenius parameters [33] of di-ester at 3.0 and 5.0 mol. dm⁻³ HCl. The magnitude of Arrhenius parameters fall in the range at bimolecular nature of hydrolysis. The value of activation energy (E) is very low i.e. < 25 kcal mol⁻¹, the value of entropy of activation (ΔS[‡]) is negative and frequency factor (λ) has power less than 12. Hence, the reaction proceeds bimolecularly via conjugate acid species.

TABLE 5 ARRHENIUS PARAMETER FOR THE RATE OF HYDROLYSIS OF DI-5- CHLORO, 2-METHYL ANILINE PHOSPHATE VIA CONJUGATE ACID SPECIES AT 80°C.

HCl (mol dm ⁻³)	Parameters		Entropy – ΔS [‡] (e.u)
	Energy of activation (E) Kcal. mole ⁻¹	Frequency factor (λ) (sec ⁻¹)	
3.0	21.50	5.56 × 10 ⁷	20.80
5.0	21.96	7.30 × 10 ⁸	20.30

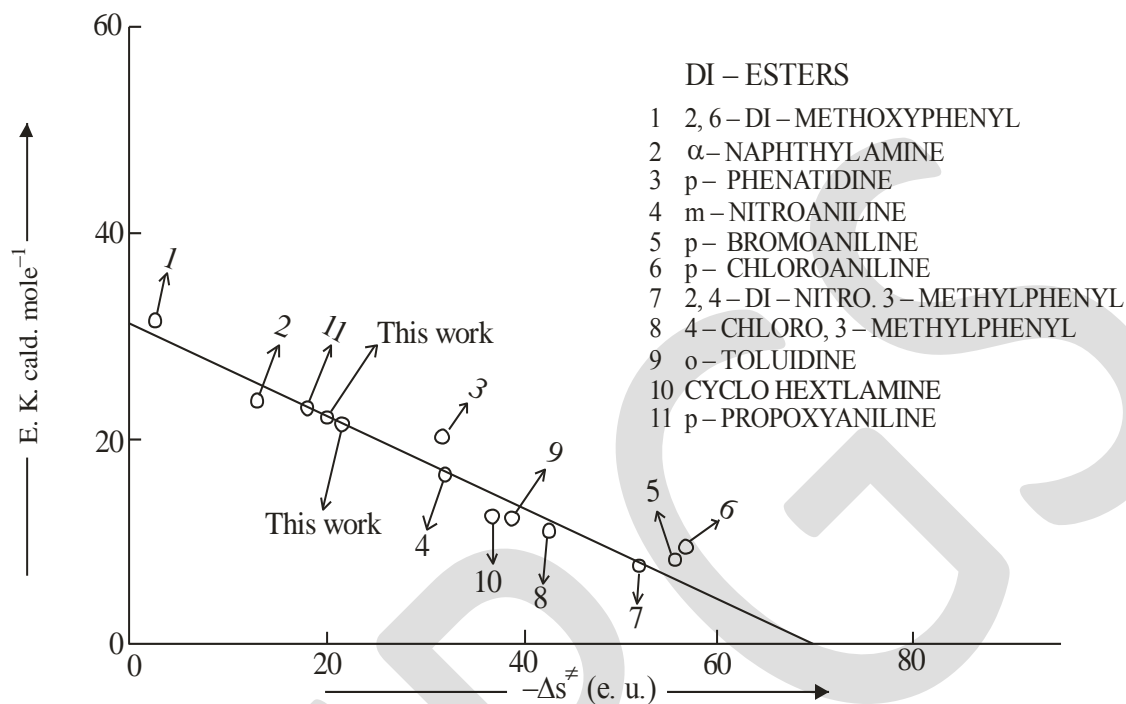
Table 6 describes the comparative isokinetic rate data of some other similar substituted phosphate diesters (the bond-fission and molecularity of which are known). Fig V shows isokinetic relationship of 5-chloro, 2-methyl aniline phosphate diester with some other phosphate diesters. The linearity of the curve shows similarity of mechanism of present diester with other diesters of known mechanism, since the point at 5-chloro, 2-methyl aniline phosphate diester lies on the same line of other phosphate diester. Thus, 5-chloro, 2-methyl aniline phosphate diester undergo bimolecular hydrolysis with P-N bond fission.

TABLE 6: COMPARATIVE ISOKEINETIC DATA RATE DATA FOR THE HYDROLYSIS OF SOME PHOSPHATE DIESTER VIA THEIR CONJUGATE ACID SPECIES

S. No.	Phosphate di-ester	Temp °C	Medium	E.K. (cals/mole.)	- $\log S^\ddagger$ (e.u)	Bond fission	Molecularity	Reference
1.	2,6-di-methoxy phenyl	98	-	31.56	2.57	P-O	-	34
2.	\square -naphthyl amine	98	2.5	23.57	12.71	P-N	2	35
3.	p-phenatidine	98	3.0	20.55	31.84	P-N	2	36
4.	m-nitroaniline	98	3.0	16.61	31.90	P-N	2	35
5.	p-bromoaniline	50	3.0	9.15	55.98	P-N	2	37
6.	p-chloroaniline	90	3.0	9.15	56.78	P-N	2	37
7.	2, 4-dinitrodi phenylamine	25	3.0	7.59	52.5	P-N	2	38
8.	4-chloro, 3,5, di-methylphenyl	98	-	29.75	22.02	P-O	-	39
9.	o-toluidine	50	1.0	11.49	38.66	P-N	2	40
10.	Cylohexyl amine	50	5.0	12.09	37.11	P-N	2	41
11.	p-propoxyaniline	97	3.0	23.79	17.98	P-N	2	42
12.	5-chloro, 2-methyl-aniline	80	3.0	21.50	20.80	P-N*	2	This work
		80	5.0	21.96	20.30	P-N*	2	This work

* Bond fission assumed

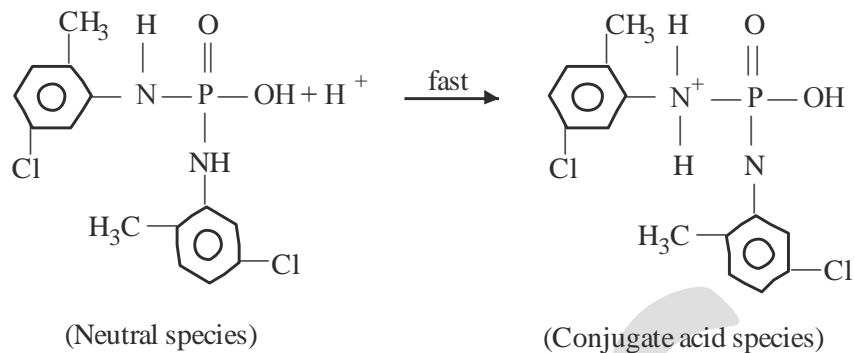
FIG.V **COMPARATIVE KINETIC RATE DATA FOR THE HYDROLYSIS OF SOME PHOSPHATE DI-ESTERS VIA THEIR CONJUGATE ACID SPECIES**



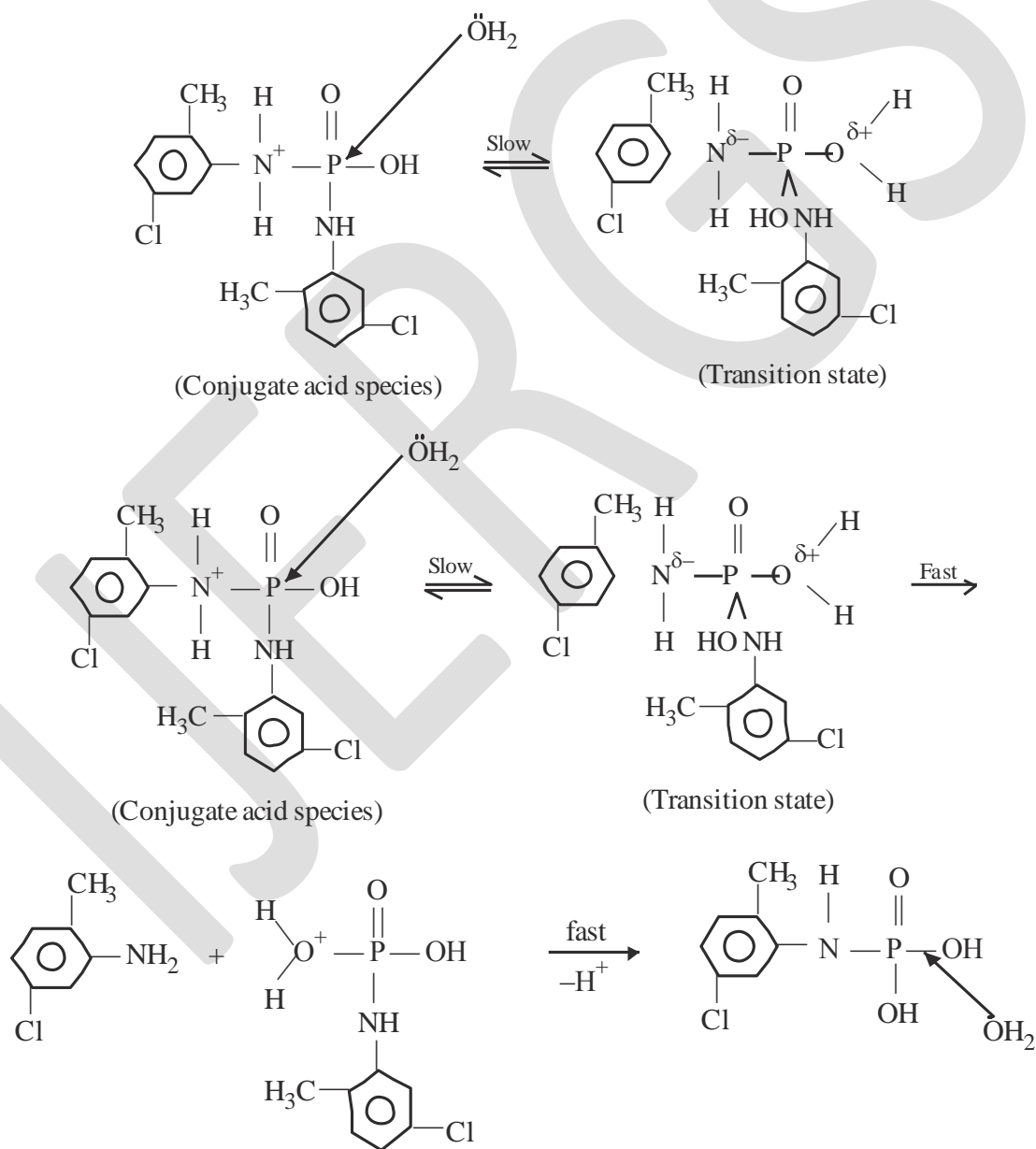
Bimolecular mechanism of 5-chloro, 2-methyl aniline phosphate diester is also supported by Hammett relationship [43-45] (Slope value = 0.31), Zucker-Hammet plot [46] (Slope value = 0.66), Bunnett plot [47,48] (slope value $\rho = 10.0$ and $\rho^* = 5.0$) and Bunnett-olsen plot [49] ($\rho = 1.63$) (Figs. not shown)

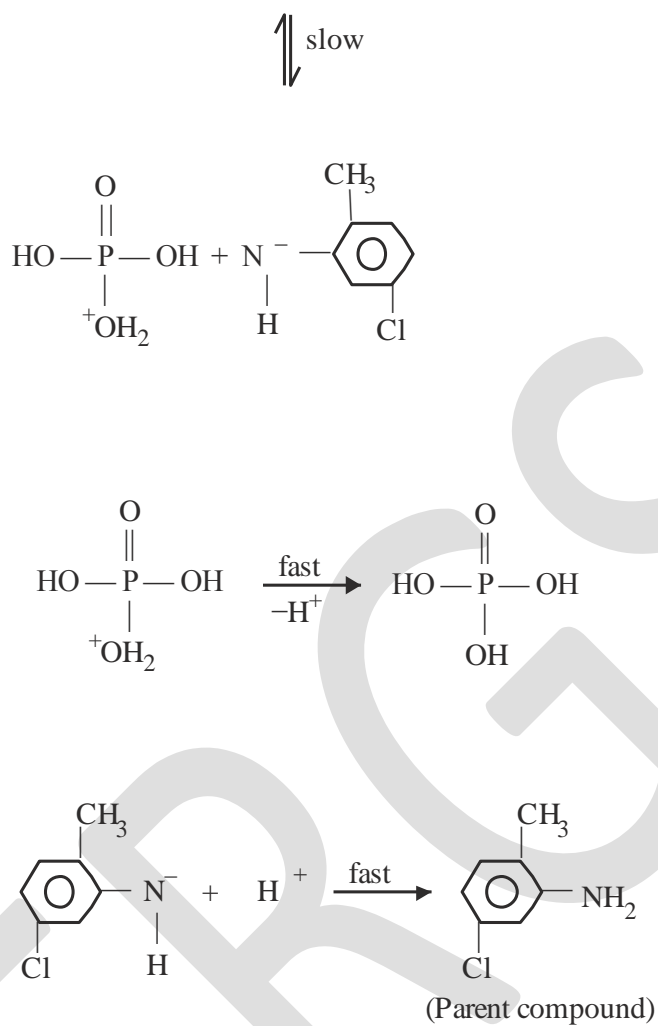
MECHANISM : Taking into account all the above consideration, the most probable reaction path via conjugate acid species of di-5chloro, 2-methyl aniline phosphate ester may be formulated as

(I) Formation of conjugate acid species by fast pre equilibrium Proton transfer :



(II) Bimolecular heterolysis of conjugate acid species involving P–N bond fission S_N2 (P) :





REFERENCES:

1. Allen, R.J.L., *Biochem J.* (34), (1940)
2. Cox, J.R. and Ramsay, O. B., *chem. Rev.* (64) No.4, 317-352 (1964).
3. Mejia-Radillo, Yamilet-Yastsimisky. Anatoly, K., *Inorganic Chemica. Acta, Vol.* (328), 241-246 (2002).
4. Tiwari, B.K, Chaudhary, A. and Dixit, D.K., *Acta Ciencia Indica, vol* (XXIVC) No 1, 015 (1998)
5. Tewari, B.K., Ph.D. Thesis, Agra Univ., Agra (1985).
6. Kumar, Abanish, Ph.D. Thesis, Dr. B.R.A. Univ., Agra (2013)
7. Kumar, Raman, Ph.D. Thesis, Dr. B.R.A., Univ. Agra (2013).
8. Verma, Devdutt, Ph.D. Thesis, Dr. B.R.A., Univ. Agra (2013)
9. Shindhe, C.P., Nikam, A.R. and Mhala, M.M., *Acta Ciencia Indica, Vol.* (XIIC), No. 1, 46 (1986).
10. Kushwaha, R.S., Tiwari, B.K., Singh, P., Upadhayaya, S and Sharma Indu Shekhar, *Journal of Indian Council of Chemists, Vol.* (IV), No. 3 (1988).
11. Singh Archana and Prabha, Shashi, *Asian J. of Chem.* Vol (8) No. 1, 129-133 (1996).
12. Saxena, Amrita, Ph.D. Thesis, Dr. B.R.A. Univ., Agra (2014).
13. Singh, Sanchita, Ph. D. Thesis, Dr. B.R.A. Univ., Agra (2014).
14. Singh, Pratap and Kumar, Abanish, *J. of Indian council of Chemists, Vol* (28) No. 1 P- 56-69 (2011).
15. Chaudhary, Gaurav, Ph.D. Thesis, Dr. B.R.A. Univ., Agra (2013).
16. Patel, Anil, Ph.D. Thesis, Dr. B.R.A. Univ., Agra (2012).
17. Tiwari, B.K., Agarwal (Miss) Anupam, Parihar, P.S., Dixit, V.K., Kadam (Miss) Rishika, Singh, R. and Singh, P., *Asian Journal of Chem., Vol.* (18), No. 4 (2006).
18. Tiwari, B.K., Chaturvedi, K. and Chaudhary, A., *Acta Ciencia. Indica, Vol* (XXVIC), No.2, 053 (2000).
19. Singh, R.K. and Gupta, Ruchi, *Acta Ciencia Indica, Vol.* (XXIVC), No. 1, 055 (2003).
20. Tiwari, B.K., (Miss) Kanta, Solanki, (Miss) Ashita, David (Miss) Shweta, Rajput, R.P. *Acta Ciencia Indica, Vol* (XXVIIC), No. 3, 113-124 (2001).
21. Tiwari, B.K., solanki (Miss) Ashita, David (Miss) Shweta, (Miss) Kanta, Sharma, Ajay, *Acta Ciencia Indica, Vol.* (XXVIIC). No. 3, 129-141 (2001).
22. *The Chemistry of organophosphorous Pesticides Fert.*, K.J. Schimidt, Springer Verlog Berlin Heideiberd, New York (1973).
23. Metcalf, R.L., *Organic pesticides*, Interscience publishers, New York, Chapter (XI), 255-261 (1955).
24. *Chemical Abstrat*, No. (154), 1993 : (1960).
25. Schrader, G., Entwicklung newer, "Insecticide of Grudlaye Organischerflour and Phophoverbi no dungen." Verlag Chemic, Winheim, Bergster (1952).
26. Schlesinger, A.H., C.A., (49) 5517° (1955).

27. Maquire, M.H. and shaw, G.J., *Cheam. Soc.*, 1979–82 (1953).
28. Barnard, P. W.C., Bunton, C.A., Killerman, D., Mhala, M.M. Silver, B., Vernon, C.A. and Welch, V.A., *J. Chem. Soc., Sec (B)*, 227–235 (1966).
29. Paul Otto. Ber., (28), 816 (1895).
30. Rudert, P., Ber., (26), 565 (1893).
31. Bronsted, J., *Z. Physik, Z. Chem.*, (102), 169 (1992); (115), 237 (1925).
32. Bjerrum, N., *Z. Physik, Z. Chem.*, 108, 82 (1924) ; 118, 251 (1925).
33. Arrhenius, S., *Z. Physik chem.*, 4 226 (1989).
34. Prabha (Miss.), Shashi, Ph. D. Thesis, Jiwaji Univ. Gwalior (1971).
35. Bhoite, A.K., "*Kinetic study of hydrolysis of compds.containing C,N and P (C-N-P) Linkage*" Ph.D. Thesis, Jiwaj Univ., Gwalior (1977).
36. Kulshrestha, K., Ph. D. Thesis, Jiwaji Univ., Gwalior (1982).
37. Bhadoria, Singh, K.A., Ph. D Thesis, Jiwaji Univ., Gwalior (1982).
38. Dubey, R., Ph. D. Thesis, Jiwaji Univ., Gwalior (1993).
39. Kushwaha, R.S., Ph.D. Thesis, Jiwaji Univ., Gwalior (1980).
40. Sagne, A.N., Ph. D. Thesis, Jiwaji Univ., Gwalior (1972).
41. Chauhan, K.P.S., Ph. D. Thesis, Jivaji Univ., Gwalior (1977).
42. Chaudhary, Amit., Ph.D. Thesis, Dr. B.R.A. Univ., Agra (1998).
43. Hammett, L.P., "*Physical Organic Chemistry*", McGraw-Hill Book Co. Ltd., London, 273 (1940).
44. Hammett, L.P. and Dyrup, A.J., *J. Am. Chem. Soc.*, (54), 2721 (1933).
45. Long, F.A. and Paul, M.A., *Chem. Revs.*, (57) (1957).
46. Zucker, L. and Hammett, L.P., *J. Am. Chem. Soc.*, (61) 2779–2785 (1939).
47. Bunnett, J.F. *J. Am. Chem. Soc.*, (83). 4956, 4968, 4973, 4978 (1967).
48. Bunnett J.F. "*Technique of Organic Chemistry*", Vol III ed. A weisaberger, "*Rates and mechanism of reactions*" Part (I), Ch VI., Pg. 177 (1961).
49. Bunnett J.F. and Olsen F.P., *Canada. J. Chem.*, (44) 1971 (1966).