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Kinetic Studies on the Electrophilic Chlorination of Certain Aryl Ethers in Solution Using 1-Chlorobenzotriazole

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Extensive kinetic investigations have been carried out on the electrophilic chlorination of nine aryl ethes in acetic acid solution by 1-chlorobenzotrizole. The total order of the reaction, order in substrate and order in 1-chlorobenzotriazole are determined. the stoichiometry of 1-chlorobenzotriazole-4-bromoanisole reaction is found to be 1 : 1. The activation energies are determined for these reactions and explained on the basis of the structure of substrate molecules. The product analysis has been carried out under kinetic concentrations using ^{1}H NMR spectrum. The influence of perchloric acid and benzotriazole added on the rate of the reactions are studied. The activation energy values are correlated with total electron density at the reaction site and the ionization energies of the molecules computed by MOPAC calculation at PM3 level. Based on the kinetic results a suitable mechanism has been proposed.

Key Words: Kinetics, Electrophilic chlorination, Aryl ethers, 1-Chlorobenzotriazole.

INTRODUCTION

1-Chlorobenzotriazole (1-CBT) has been widely used as the oxidant for a number of organic substrates[1-3]. Molecular chlorine[4], N-halosuccinimide[5] and N-chloroacetanilide[6] are commonly used chlorinating agents in solution. Kinetic studies on the chlorination of several organic substrates by these reagents have been extensively carried out. 1-Chlorobenzotriazole can be used in polar medium as the source of Cl^+ and it can be conveniently used as the chlorinating agent for aromatic compounds[7, 8] like aryl ethers. There are few reports on the use of 1-CBT as the chlorinating agent[9]. Detailed kinetic investigations have not been reported even in these limited studies. The present work deals with an extensive kinetic investigation on the chlorination of nine aryl ethers in aqueous acetic acid solution using 1-CBT.

EXPERIMENTAL

The substrates were Fluka sample of anisole (b.p. 154°C), 4-methylanisole (b.p. 174°C), 4-chloroanisole (b.p. 198°C), 4-bromoanisole (b.p. 223°C), 4-fluoroanisole (b.p. 155°C), 4-nitroanisole (m.p. 54°C), phenetole (b.p. 170°C), 4-chlorophenetole (b.p. 212°C) and biphenyl ether (b.p. 259°C). The substrates were so chosen that there would be wide variation in the reactivity.

Fischer AR grade glacial acetic acid was further purified by the method of Orton and Bradfield[10]. Aqueous acetic acid, *i.e.*, 90, 75 and 50% were prepared by mixing appropriate volumes of double distilled water and dry acetic acid.

1-Chlorobenzotriazole (1-CBT) was prepared by treating benzotriazole in aqueous acetic acid (50% v/v) with sodium hypochlorite solution[11]. The solid formed was extracted with chloroform, then washed with water and dried over anhydrous magnesium sulphate. The crude 1-CBT was recrystallized from a mixture of *n*-hexane chloroform (m.p. 103–106°C).

A stock solution (0.16 M) was prepared and diluted to the required concentration. The 1-chlorobenzotriazole solution was used on the same day. AnalaR samples of sodium thiosulphate, potassium iodide and starch were used for titrations. AnalaR grade perchloric acid was used as catalyst in some reactions.

Kinetic measurements: The kinetic runs were carried out at constant temperature maintained by Hippler type ultrathermostat (VEB Prufgerate Werk, Germany) with an accuracy of ±0.1°C. The rate measurements of these reactions were followed by iodimetric titrations. The stoichiometry of the reaction between 1-CBT and 4-bromoanisole was determined under kinetic concentrations. The stoichiometry of 1-CBT-4-bromoanisole reaction was found to be 1 : 1. It may be assumed that the stoichiometry is same for other reactions also.

Product analysis: In the present work, the product formed in the reaction of 1-CBT with anisole in the concentration range 10^{-2} M was carefully analyzed and identified as 4-chloroanisole using the ^{1}H NMR spectrum.

^{1}H NMR spectrum of anisole is presented in Fig. 1 (a) while Fig. 1 (b) is that of the product formed in CBT-anisole reaction. The absorption at $\delta = 1.6$ ppm

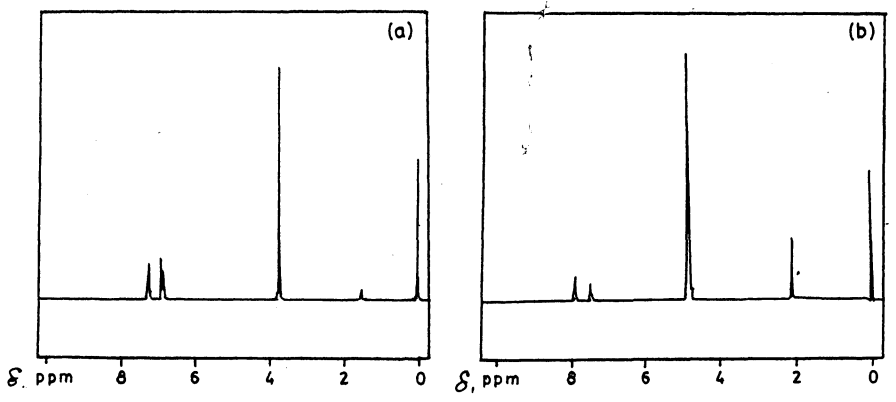
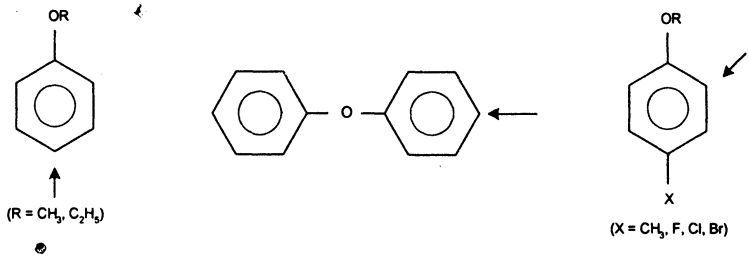


Fig. 1. (a) ^{1}H NMR spectrum of anisole, (b) ^{1}H NMR spectrum of product obtained from anisole-CBT reaction

[Fig. 1 (a)] is due to the methoxy methyl protons while the aromatic protons of anisole gave signals at $\delta = 6.8$–7.6 ppm. The PMR spectrum of the product [Fig. 1 (b)] contains a singlet at $\delta = 2.0$ ppm. There are two doublets in the PMR spectrum ($\delta = 7.6$–8.0 ppm) which indicate that the product of the reaction is 4-chloroanisole. It may be pointed out that the product was analyzed at kinetic concentration (10^{-2} M) and under these conditions 4-chloroanisole was the only product.

The positions of electrophilic attack in different aromatic ether molecules are indicated below.



MOPAC calculation: In order to compare the reactivity of the substrates under investigation, an attempt has been made to correlate the experimental activation energy values with the theoretically calculated molecular properties. Total electronic charge density and ionization potentials of the substrate molecules are computed for all the substrate molecules by MOPAC calculation at PM3 level.

RESULTS AND DISCUSSION

In the present study, a detailed kinetic investigation was carried out with 4-bromoanisole. The total order of the reaction, the order with repsect to substrate and the order with respect to 1-CBT were thoroughly established in 90% aqueous acetic acid (v/v) at 303 K.

The total order of the reaction was first determined by the fractional life period method. The values of order (n) of the reactions are given in Table-1.

TABLE-1
4-BROMOANISOLE-CBT REACTION
(total order of the reaction by fractional life period method)

Solvent: 90% aqueous acetic acid (v/v) $[HClO_4] = 0.026$ M T: 303 K

% of 1-CBT reacted	$a_2/10^{-3}$, M	$a_1/10^{-3}$, M	t_2, min	t_1, min	n
20	8	4	35	70	2
30	8	4	62	120	2
40	8	4	90	170	2
20	10	4	27	70	2
30	10	4	38	108	2
40	10	4	63	160	2

The total order of the reaction was also determined by the method of integration. The plots of 1/(a–x) against time are shown in Fig. 2.

These plots are linear suggesting that the order of the reaction is two. The constancy of second order rate constant values proves that the overall reaction is second order in 1-chlorobenzotriazole-4-bromoanisole reaction at 303 K in acetic acid solution at constant $[HClO_4]$.

Under pseudo-first-order condition of [S] > [CBT] the experimental results fitted well into the integrated first order rate equation. Plots of log (a – x) against 't' for various concentrations of 4-bromoanisole in 90% aqueous acetic acid (v/v) at 303 K are shown in Fig. 3.

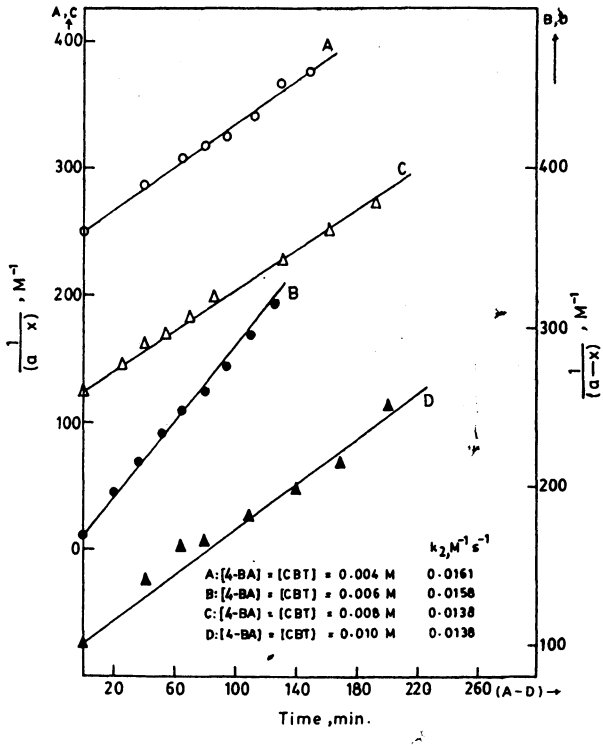


Fig. 2. 4-Bromoanisole-CBT reaction; Plots = $\frac{1}{(a-x)}$ *vs.* time. $[HClO_4] = 0.026$ M; Solvent: 90% aqueous acetic acid (v/v); T = 303 K

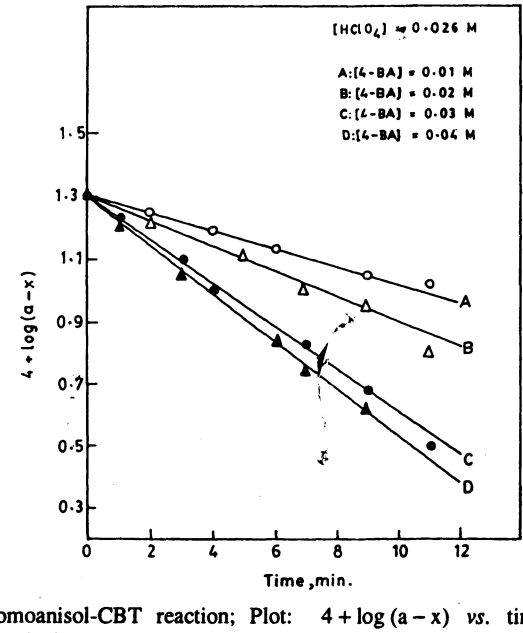


Fig. 3. 4-Bromoanisol-CBT reaction; Plot: $4 + \log(a-x)$ *vs.* time; Variation of [4-bromoanisole]; Solvent: 90% aqueous acetic acid (v/v); [1-CBT] = 0.002 M; T = 303 K

It is seen that the plots are not only linear but also give the intercept of log (a). From these slopes of these lines the pseudo-first-order rate constant k_1' was calculated. These k_1' values are used to establish the order with respect to substrate. The values of k_1', log k_1' and log [4-bromoanisole] are given in Table-2.

TABLE-2
4-Bromoanisole-CBT REACTION VARIATION OF [4-BROMOANISOLE]

Solvent: 90% aqueous acetic acid (v/v); $[HClO_4] = 0.026$ M; [1-CBT] = 0.002 M; T: 303 K

[4-bromoanisole], M	$k_1'/10^{-4}$ s^{-1}	4 + log k_1'	2 + log [4-bromoanisole]
0.01	4.44	0.6474	0.0000
0.02	8.33	0.9206	0.3010
0.03	11.36	1.0553	0.4771
0.04	14.44	1.1596	0.6021

Plots of log of k_1' against log [4-bromoanisole] are shown in Fig. 4.

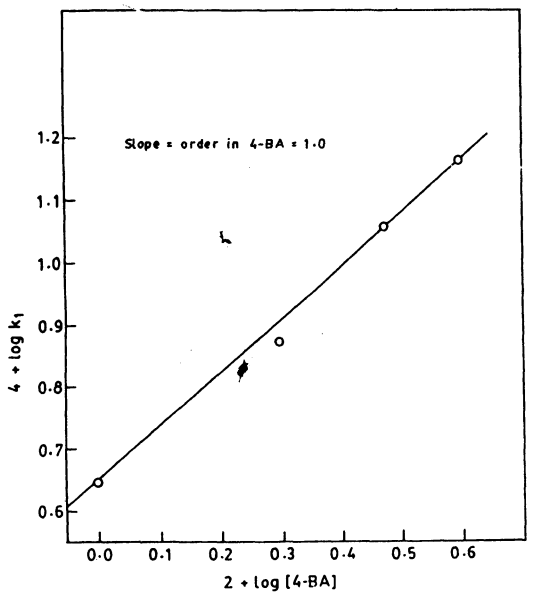


Fig. 4. 4-Bromoanisole-CBT reaction; Plot: 4 + log k_1' *vs.* 2 + log [4-bromoanisole]; Variation of [4-bromoanisole]; Solvent: 90% aqueous acetic acid (v/v); [1-CBT] = 0.00 M; T = 303 K; $[HClO_4] = 0.026$ M.

From the slope value the order with respect to substrate was found to be one.

The order with respect to 1-CBT was determined by differential method. Series of runs in which [S] was kept constant and in excess and [1-CBT] was varied, was carried out. For each run $\{-d[1\text{-CBT}]/dt\}_0$ was evaluated from the concentration-time curve.

Fig. 5 (B) shows the plot of log $\{-d[1\text{-CBT}]/dt\}_0$ against log [S]. The slope of this line is 0.9, indicating that the reaction is first order with respect to 4-bromoanisole. plot of log $\{-d[1\text{-CBT}]/dt\}_0$ against log [1-CBT]) is linear with a slope of unity (Fig. 5A). This confirms that the order with respect to 1-CBT is one.

Chlorination of 4-bromoanisole in aqueous acetic acid by 1-CBT was catalyzed by perchloric acid. In order to propose a suitable mechanism for the acid catalyzed chlorination of aryl ethers, the effect of [$HClO_4$] on the rate of the reaction was studied. It is found that the increase in [$HClO_4$] increases the rate of the reaction.

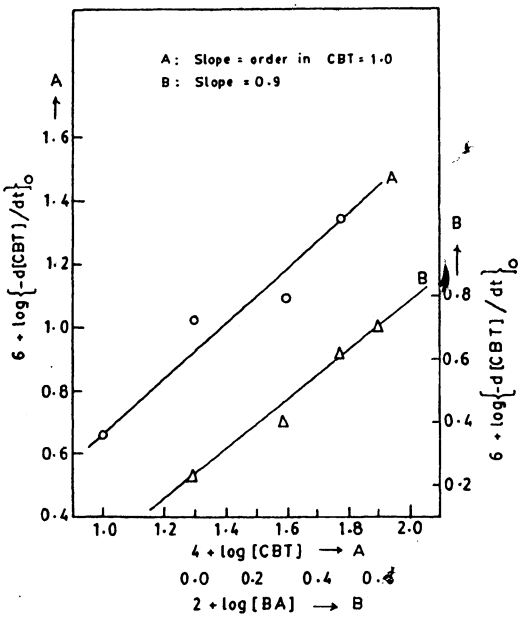


Fig. 5. 4-Bromoanisole-CBT reaction; (a) Plot: 6 + log $\{-d[1\text{-CBT}]/dt\}_0$ *vs.* 4 + log [1-CBT]; (b) Plot: 6 + log $\{-d[1\text{-CBT}]/dt\}_0$ *vs.*2 + log [BA]; Variation of [1-CBT]; Solvent: 90% aqueous acetic acid (v/v); [4-bromoanisole] = 0.04 M; T = 303 K; [$HClO_4$] = 0.026 M

Plots of log k_2 against log [$HClO_4$] is given in Fig. 6. From slope value of that linear plot it is evident that the order with respect to [$HClO_4$] is found to be two.

Benzotriazole (BT) is one of the products formed in the reaction between 4-bromoanisole and 1-CBT. The influence of added [BT] on the rate of the reaction was studied and found that the addition of benzotriazole decreases the rate of the reaction. The values of [BT] and k_2 are given in Table-3.

TABLE-3
4-BROMOANISOLE-CBT REACTION EFFECT OF ADDED BT

Solvent: 90% Aqueous acetic acid (v/v); [$HClO_4$] = 0.026 M;
[4-bromoanisole] = [1-CBT] = 0.004 M; T: 303 K

[BT], M	4 + log [BT]	$K_2/10^{-3}$ M^{-1} s^{-1}	2 + log k_2
0.004	1.6021	23.80	0.3765
0.008	1.9030	20.00	0.3010
0.012	2.0790	14.80	0.1700
0.016	2.2041	12.50	0.0960

BT = Benzotriazole

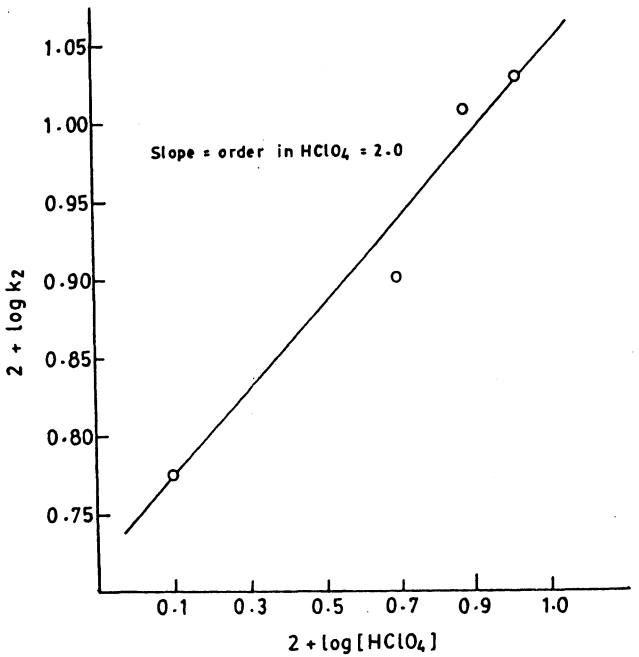


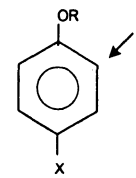
Fig. 6. 4-Bromoanisole-CBT reaction; Plots: $2 = \log k_2$ *vs.* $2 + \log [HClO_4]$; Variation of $[HClO_4]$; Solvent: 90% aqueous acetic acid (v/v) [4-bromoanisole] = [1-CBT] = 0.004 M; T = 303 K.

Reactivity of aryl ethers: The reactivity of aryl ethers in the reaction with 1-CBT can be compared with activation energy values. The activation energy values were determined by measuring the rate constants at different temperatures. The values of E_a and activation parameters are given in Table-4.

TABLE-4
ACTIVATION PARAMETERS FOR THE CHLORINATION OF CERTAIN AROMATIC ETHERS USING 1-CHLOROBENZOTRIAZOLE

Compound	k_2 ($M^{-1} s^{-1}$) at 303 K	log A	E_a (kJ mol^{-1})	$\Delta H^{\#}$ (kJ mol^{-1})	$\Delta S^{\#}$ (JK^{-1} mol^{-1})	$\Delta G^{\#}$ (kJ mol^{-1})
Anisole	2.020	11.5	68.7	66.4	-21.3	73.0
4-Methylanisole	0.650	10.0	60.0	57.5	-59.0	75.3
Phenetole	1.860	10.6	65.4	65.0	-26.4	73.0
4-Fluoroanisole	0.035	11.3	76.4	76.0	-20.0	82.4
4-Chloroanisole	0.039	11.6	77.7	75.2	-25.3	85.4
4-Chlorophenetole	0.033	10.4	71.5	67.0	-53.4	83.2
4-Bromoanisole	0.016	10.7	74.6	72.2	-41.3	84.7
Diphenyl ether	0.510	11.6	71.6	69.0	-23.0	76.0
4-Nitroanisole	0.001	12.0	90.0	88.4	-15.0	92.9

Solvent: 1–3: Dry acetic acid; 4–8: 90% aqueous acetic acid (v/v)
9: 50% aqueous acetic acid (v/v)



$R = CH_3, C_2H_5$
$X = CH_3, F, Cl, Br, NO_2$

The main aim of choosing these six substrates is to compare the ortho reactivities of the para substituted aryl ethers containing both electron releasing and electron withdrawing substituents. In all these six substrates electrophilic chlorination occurs at meta position with respect to the substitutent and ortho to the ether group as indicated.

Earlier workers[12] have used the additivity principle ot determine the meta reactivities of deactivating substituents (X) in halogenation of anisoles. Generally, an activating substituent is placed in such a position that the reactivity of the deactivated meta position is increased and it is assumed that the effect of the activating substituent remain constant throughout the reaction series. By examining the rates of positive halogenation of anisoles of the above type, Branch and Jones[13] have found that the *m*-fluoro substituent is less deactivating than *m*-chloro which is several times deactivating than *m*-nitro substituents. In the present investigation, the E_a values for the six para substituted anisoles are in the following order:

4-Methylanisole < 4-chlorophenetole < 4-bromoanisole

$\simeq$ 4-chloroanisole < 4-fluoroanisole < 4-nitroanisole

This trend in E_a values suggests that the total electron density at 2 position in 4-methylanisole is the highest among the six molecules. Thus, methyl group activates the meta position in aryl ethers. Among the 4-haloanisoles, the electron density at the reaction site is less in 4-fluoroanisole while in 4-chloroanisole and 4-bromosanisole, position 2 is equally electron rich. It may be pointed out that 4-chlorophenetole has lower E_a value than 4-chloroanisole just as phenetole has lower E_a value than ansisole. These values indicate that ethoxy group releases electron to a greater extent than methoxy group. The E_a value of 4-nitroanisole is the highest and hence the total electron density at position 2 of this molecule is the lowest among the six para substituted aryl ether molecules investigated.

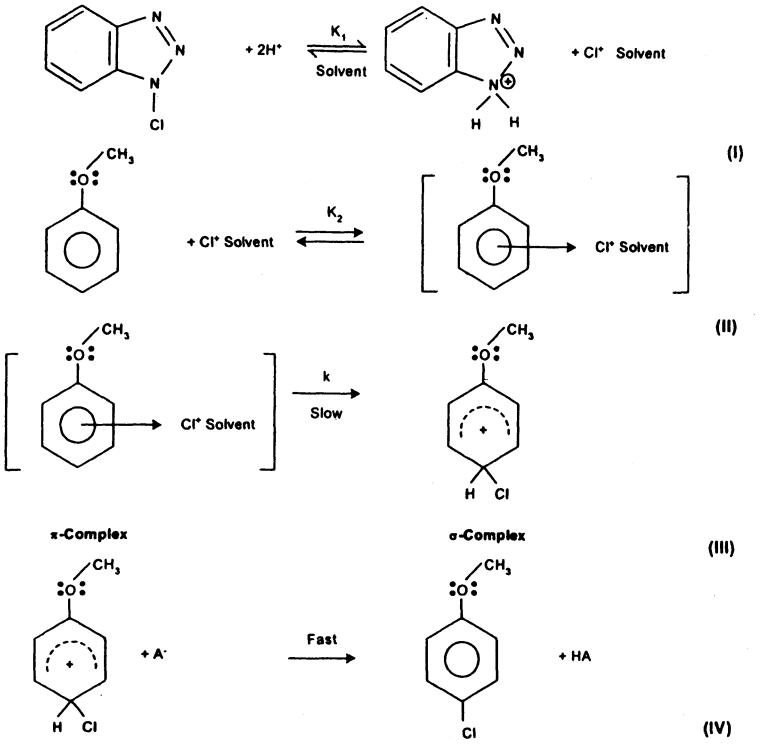
The discussion advanced for the trend in E_a values of the various aryl ethers is applicable to the trend in the $\Delta H^{\#}$ values on these two parameters which are directly related to each other. The entropy of activation $\Delta S^{\#}$ values for the chlorination of aryl ethers in acetic acid solution are negative indicating the loss of entropy when the activated complex is formed. The following explanation may be offered for this observation. The activated complex involved in the chlorination of the compounds investigated is more polar than the reactants. They are therefore, more solvated in a polar solvent than the reactants. Consequently, the entropy of the activated complex is less than that of the reactants and the values are negative. It may be pointed out that in the case of chlorination of 4-nitroanisole, $\Delta S^{\#}$ is less negative than those for the reactions of other aryl ethers. In 4-nitroanisole, the presence of polar nitro group increases the extent of solvation of reactant molecule and its entropy is reduced. With the result, the $\Delta S^{\#}$ value for this reaction is less negative than those for the chlorination of other substrates.

Mechanism

The kinetic studies on the chlorination of aryl ethers, in dry acetic acid and aqueous acetic acid by 1-CBT indicate that the mechanism of chlorination of

these compounds with 1-CBT is similar to that of chlorination of molecular chlorine.

Based on the kinetic results the following mechanism may be given for the chlorination of aryl ethers by 1-CBT dry and aqueous acetic acid solution in the concentration range 1×10^{-3}–10×10^{-3} M **(Scheme-1).**



(A⁻ : Conjugate base of the acid HA)

Scheme-1

In this scheme K_1 is the equilibrium constant for the formation of solvated Cl^+ ion from 1-CBT and H^+ and K_2 is another equilibrium constant for step (II) in which the electrophile and substrate form a 1 : 1 complex, namely π-complex. This complex in solution rearranges into σ-complex in a slow rate determining step. Since the C—H bond breaking has not made any appreciable progress in the transition state, step (IV) is also a fast step. This mechanism explains the experimental observations that the reaction is first order in anisole and first order in 1-CBT.

Correlation of charge density and ionization potential with activation energy

In the halogenation of aromatic compounds in acetic acid, the interaction between the reaction partners is electrostatic in nature. Kannappan[15] *et al.* calculated total electron density at various positions of homocyclic and heterocyclic aromatic molecules and successfully correlated the total electron density at the reaction site with the experimental activation energies obtained for the

bromination of these compounds. They also stressed the need for the inclusion of σ-charges in any meaningful correlation of charge densities with experimental data. In the present work, the electronic distributions in anisoles were computed by using the semiempirical MO method at PM3 level[16, 17]. The computations were carried out using the software MOPAC 2000[18]. The total electron densities at different ring carbon atoms of nine homocylic aromatic molecules are given in Fig. 7. These data clearly indicate that the electrophile approaches electron-rich

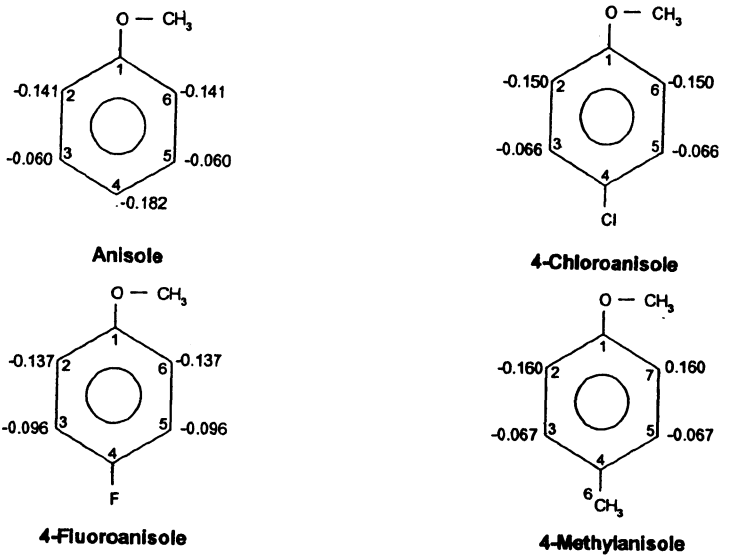


Fig. 7. Electronic distribution at various ring carbon atoms of certain anisoles

centre in these molecules. Further, there is linear coorelation between the total electron density at the reaction site and experimental activation energy (Fig. 8).

It may be noted that the total electron densities calculated by MOPAC calculations correlate satisfactorily with the experimentally measured activation energies for the chlorination of aryl ethers in acetic acid solution. Further, increase in the total electron density at the reaction site decreases the activation energy.

It has been suggested that in electrophilic substitution reactions the π-electronic cloud is polarized by the approaching electrophile. Therefore, the ease of formation of the charge transfer complex between the substrate molecule and the electrophile (1-CBT) should depend on the ionization energy of the substrate molecule. Ionization energies are calculated for all the aryl ethers used in the present investigation by MOPAC calculation at PM3 level. Fig. 9 contains the plots of experimental activation energies against ionization potential of aryl ethers. These plots are linear indicating that the experimentally determined activation energies correlate satisfactorily with the computed ionisation potential for the substrate molecules. It is expected that an aromatic molecule with high ionization energy can be polarized with difficulty and hence the formation of charge transfer complex becomes difficult. Plot in Fig. 9 shows that increase in ionization potential of substrate molecule increases the E_a value for the chlorination of these compounds.

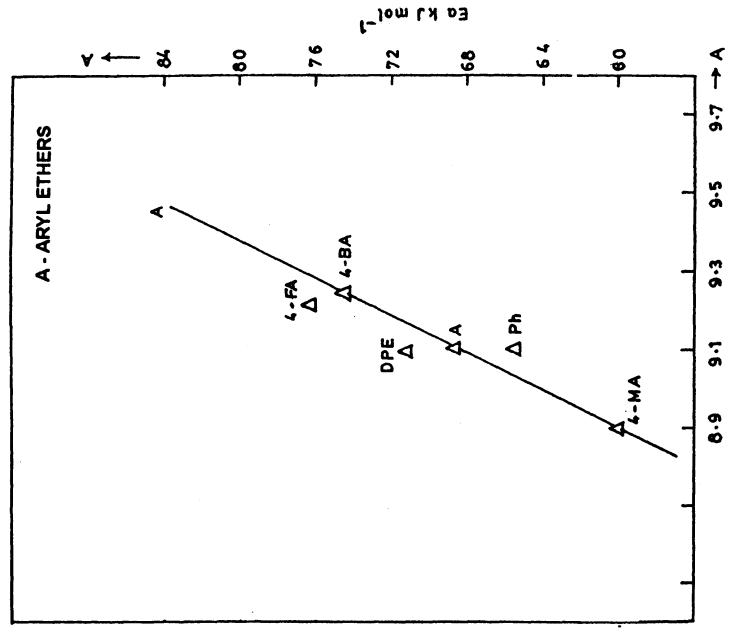


Fig. 9. Energy of activation *vs* ionization potential

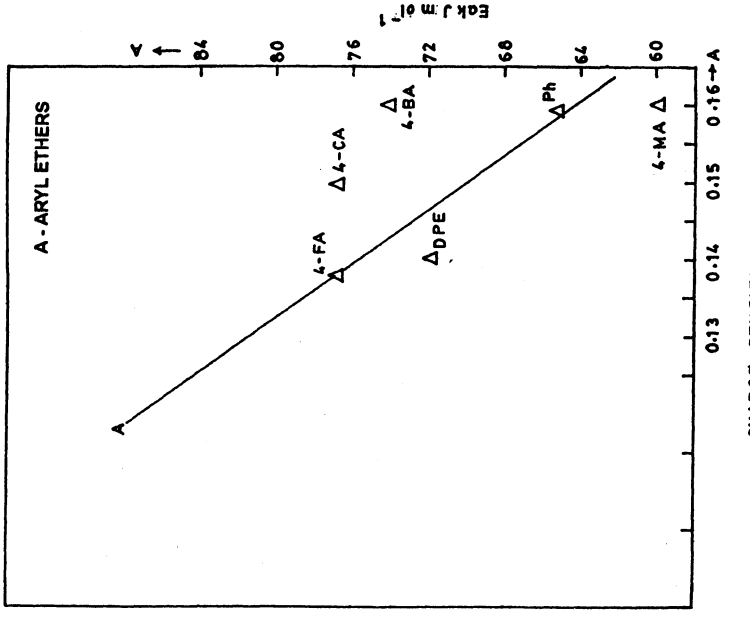


Fig. 8. Energy of activation *vs* charge density

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