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Kinetic study on the reaction of N-chlorosuccinimide with benzyl phenyl ethers in aqueous acetic acid

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ABSTRACT

Kinetics of oxidation of benzyl phenyl ethers [$C_6H_5CH_2 O C_6H_4 - X$] ;{X = H, o-Me, m-Me, p- Me, o-Cl and p-NO_2, } by N-chlorosuccinimide (NCS) in aqueous acetic acid medium in the presence of hydrochloric acid and sodium perchlorate have been investigated by iodometric method. The observed rate of oxidation is first order in both [NCS] and [HCl] and zero order in [benzyl phenyl ethers]. An increase in the dielectric constant of the medium decreases the rate. Addition of succinimide, the reduction product of NCS, has a slight retarding effect on the rate of oxidation. The reaction rate remains constant with the increase in [NaClO_4]. The stoichiometry of the reaction is found to be 1:1. It fails to induce polymerization of acrylonitrile under the experimental conditions employed. The kinetic parameters Ea, $\Delta H^{\neq}$, $\Delta G^{\neq}$ and $\Delta S^{\neq}$ have been calculated. The corresponding ester has been identified as the product of oxidation. A suitable reaction scheme is proposed and an appropriate rate law is deduced to account for the observed kinetic data.

Keywords: Benzyl phenyl ethers, N-chlorosuccinimide, Oxidation, Kinetics.
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INTRODUCTION

Ethers are widely used as additives, herbicides, pharmaceuticals, pesticides, and solvents in agriculture, in the production of cosmetics and foods, in petroleum industries, and in polymer syntheses. Because the ether bond has a high dissociation energy (about 360 kJ mol^{-1}), ether compounds are considered recalcitrant. Halogenated alkyl ethers are also used in anesthetics and polymer syntheses [1]. Functionalization at the α C – H bonds of ethers is one of the most useful reactions in organic synthesis, because it provides for the efficient preparation of various organic compounds [2]. Ruthenium tetraoxide [3], chromium trioxide [4], PhCN$_2$ N$^+$Et$_3$ MnO$_4$ [5] and trichloroisocyanuric acid [6] oxidize ethers to esters. Reactions of aryl ethers with ozone

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[7] and hydrogen peroxide [8] lead to oxidative cleavage of the ether and formation of carboxylic acids. Benzyl alcohol has been manufactured industrially by hydrolysis of benzyl chloride with sodium carbonate [9].   This process gives 10-12 % of dibenzyl ether as an unavoidable byproduct. It is possible to convert this dibenzyl ether to benzaldehyde which is a value added product. It has been reported that oxidation of dibenzyl ether to benzaldehyde with dilute nitric acid becomes economically viable route for the manufacture of benzaldehyde.   Kinetic investigations involving oxidation of benzyl ethers by N-bromonicotinamide [10], N-chloronicotinamide [11], N-bromosuccinimide [12,13], cobaltic salts [14],   nitric acid [15], permanganate [16], 2,3 dichloro-5,6 dicyanobenzo quinone (DDQ) [17], dimethyl dioxirane [18] and pyridinium fluorochromate [19] have been reported.

Some specific features of N-halo succinimides determine their wide application in organic synthesis. N-halo succinimides are sources of positive halogens and these reagents have been exploited as oxidants for a variety of substrate [20]. This is due to the high lability of the N-X bond and various modes of its splitting. Depending on the conditions, a number of highly reactive intermediates can be formed: halogen radicals, halogen cations, halogen anions, N-radicals, N-cations, N-anions, etc. As a result , N-halo succinimides promote very important reactions, such as halogenations, solvolytic halogenations, imidation, oxidation, as well as other processes resulting in the formation of compounds with C-X, C-O, C=O, S-X, P-X, C-N, P-N, S-N, S=N, etc.,

N-Chlorosuccinimide (NCS) is a versatile reagent and its significance is not limited to chlorination and oxidation [21]. It is used as a source for chlorine in radical reactions and various electrophilic additions. It mediates or catalyzes many chemical reactions, including halocyclizations, formation of heterocyclic systems, formation of new carbon-carbon bonds, rearrangements and functional group transformations. It can be used as pharmaceutical intermediates, organic synthesis chlorinating agent. It can also be used to prepare rubber additives, antibiotic drug intermediates. N-Chlorosuccinimide is also used as an intermediate or a chlorinating agent in the synthesis of pharmaceuticals, especially tetracycline antibiotics. NCS is a source of positive halogen and the reagent has been exploited as oxidant for a variety of substrates. Kinetics and mechanism of oxidation of benzylamines [22], dimethylsullphoxide [23], allyl alcohol [24], amino acids [25], primary alcohols [26], aromatic aldehydes [27] and ethylenediaminetetra acetic acid [28] by NCS have been reported.

EXPERIMENTAL SECTION

Methods and materials
Benzyl ethers, viz. Benzyl phenyl ether, Benzyl o-methylphenyl ether, Benzyl m-methylphenyl ether, Benzyl p-methylphenyl ether, Benzyl o-chlorophenyl ether were prepared from the corresponding alcohols and benzyl chloride by Williamson's synthesis. Benzyl p-nitrophenyl ether was prepared by the conventional reflux of p-nitrophenol, sodium hydroxide and benzyl chloride [29]. Benzyl phenyl ethers were characterized by IR spectral studies; IR (KBr, cm^{-1}): 3045, 1540, 1500, 1490, 1090.

Commercial sample of NCS was used as such. Standard solution of NCS was prepared in water and its purity was checked iodometrically.   Acetic acid (Analar, BDH) was purified by standard

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method. The solutions of the benzyl ethers were prepared in acetic acid. Hydrochloric acid (AnalaR) was used as a source of [H$^+$]. Conductivity water was used throughout the studies.

Kinetic measurements:
The kinetic runs were carried out under pseudo first order conditions ([benzyl phenyl ethers]>>[NCS]). Rate studies were carried out at a constant temperature. All the solutions were thermo stated for 30 minutes before mixing. Requisite amounts of NCS, benzyl ether solution, hydrochloric acid, sodium perchlorate and aqueous acetic acid were taken in the jena glass reaction vessel and placed in a water thermostat, maintained at the desired temperature . The course of the reaction was followed by pipetting out 3 ml aliquot of the reaction mixture at various intervals of time and analyzing the oxidant concentration iodometrically.

Stoichiometry and product analysis:
 The reaction mixture containing excess of NCS over benzyl phenyl ether in the presence of HCl and NaClO$_4$ was kept at room temperature for 36 hours. Estimation of unreacted NCS showed that one mole of benzyl ether reacted with one mole of NCS.

For product study, the substrate was taken in excess compared to that of NCS. The reaction was allowed to proceed to completion by keeping it in a thermostat at 45°C for about 3-4 h. After that, the solution was cooled and shaken with ether. The two layers were separated. The ether layer was washed with water several times. It was dried with anhydrous sodium sulphate. The corresponding ester has been identified as the major product of oxidation by spot tests and IR.

RESULTS AND DISCUSSION

At constant [HCl] and [NaClO$_4$] with the [benzyl ether] in excess, the plot of log k$_{obs}$Vs time is linear, indicating first order dependence of rate on [NCS]. The rate of the reaction remains constant with the increase in [benzyl ether], indicating zero order dependence on substrate concentration (Table 1).

The pseudo-first order rate constant increases with increase in HCl in the range 0.05 – 0.20 M (Table 1) and the plot of log k$_{obs}$ Vs log [HCl] is linear with slope unity (r = 0.99). The effect of H$^+$ is investigated in the range 0.05 – 0.20 M of HClO$_4$ at constant [NaCl] and the rate increases proportionately with increase in [H$^+$]. The plot of log k$_{obs}$ Vs log [H$^+$] is linear with unit slope. The effect of Cl$^-$ on the rate of the reaction is also studied by increasing the [NaCl] in the range 0.05 – 0.20 M at constant [HClO$_4$]. It has been observed that the order with [Cl$^-$] is also one, as evident from the linear plot of log k$_{obs}$ Vs log [NaCl] with a unit slope.

The effect of ionic strength on the rate of the reaction is studied by increasing [NaClO$_4$] at constant [HCl]. It has been observed that the reaction rate remains constant (Table 1) with increase in [NaClO$_4$] . Hence NaClO$_4$ act as inert salt, maintaining constant ionic strength.

An increase in the rate constant is noticed on decreasing the dielectric constant of the medium (Table 1). Plot of log k$_{obs}$ Vs 1/D, where D is the dielectric constant of the medium, gives straight line (r = 0.99) with positive slope for different benzyl ethers.
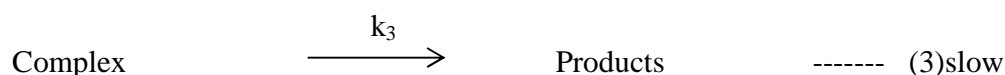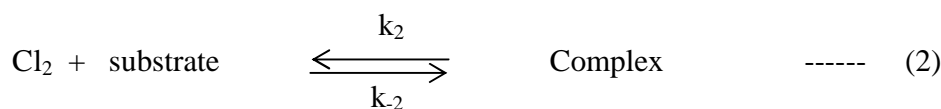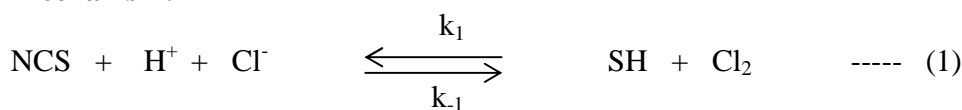
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Effect of added succinimide (SH) is studied at different initial concentrations of succinimide. It has a slight retarding effect on the rate of oxidation.

The oxidation of all the benzyl ethers has been studied at different temperatures (323-338 K). The Arrhenius plot of log k_{obs} Vs 1/T is linear. From the plot, the Arrhenius and thermodynamic activation parameters are evaluated (Table 2).

Mechanism:
The active oxidizing species has to be identified, before suggesting a most probable mechanism. The nature of the active oxidizing species and the mechanism depend on the nature of the halogen atom, the groups attached to the nitrogen and the reaction condition. The species responsible for such oxidizing character may be different depending on the pH of the medium. Under the experimental conditions studied Cl_2, HOCl, H_2OCl^+ $NCSH^+$ and NCS itself in aqueous solution can be the possible oxidizing species. It has been reported in the case of N-halo oxidants that, HOCl is the reactive oxidant species [30,31]. The participation of hypohalous acidium ion [32] in many electrophilic substitution and oxidation reactions is well observed. If $NCSH^+$ is the active oxidant, the reaction must show hydrogen ion catalysis only. Since both hydrogen and chloride ions are found to catalyse the reaction in the present case, molecular chlorine has been assumed to act as the effective oxidant. It has been reported that in aqueous acidic solutions in presence of chloride ion, NCS produces a steady, but small, concentration of molecular chlorine [33-37].

Mechanism:

$$NCS + H^+ + Cl^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} SH + Cl_2 \quad\quad ----- \quad (1)$$

$$Cl_2 + substrate \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} Complex \quad\quad ------ \quad (2)$$

$$Complex \xrightarrow{k_3} Products \quad\quad ------- \quad (3)slow$$

Rate = k_3[Complex]   --------   (4)

Applying steady-state approximation to the molecular chlorine and the complex, the following rate law is deduced.

$$Rate = \frac{k_1 k_2 k_3 \,[Substrate]\,[NCS]\,[H^+]\,[Cl^-]}{k_{-2} + k_3 \{k_{-1}[SH] + k_2[substrate]\}} \quad\quad -------- \quad (5)$$

Assuming $k_{-1}[SH] \ll k_2[substrate]$

$$Rate = \frac{k_1 k_3 \,[NCS]\,[H^+]\,[Cl^-]}{k_{-2} + k_3} \quad\quad --------- \quad (6)$$

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Equation (6) accounts for the first order dependence of rate on [NCS], [HCl] and zero order dependence on [substrate].

Table-1: Rate constants for the oxidation of benzyl phenyl ether by NCS at 318 K:

[Benzyl phenyl ether] $x10^2$ M	[NCS] $x10^3$ M	$CH_3COOH - H_2O$ % (v/v)	[HCl] x 10 M	[NaClO$_4$] x 10 M	$k_{obs} x10^4 s^{-1}$
2.0	3.0	80-20	1.0	1.0	11.43
3.0	3.0	80-20	1.0	1.0	11.51
4.0	3.0	80-20	1.0	1.0	11.20
5.0	3.0	80-20	1.0	1.0	11.43
6.0	3.0	80-20	1.0	1.0	12.08
2.0	3.0	80-20	1.0	0.25	12.13
2.0	3.0	80-20	1.0	0.50	11.96
2.0	3.0	80-20	1.0	0.75	11.84
2.0	3.0	80-20	1.0	1.00	11.51
2.0	3.0	80-20	1.0	1.25	12.02
2.0	3.0	80-20	1.0	1.50	11.66
2.0	3.0	70-30	1.0	1.0	6.53
2.0	3.0	75-25	1.0	1.0	8.48
2.0	3.0	80-20	1.0	1.0	11.51
2.0	3.0	85-15	1.0	1.0	17.79
2.0	3.0	90-10	1.0	1.0	30.79
2.0	3.0	80-20	0.5	1.0	4.75
2.0	3.0	80-20	1.0	1.0	11.51
2.0	3.0	80-20	1.5	1.0	15.85
2.0	3.0	80-20	2.0	1.0	25.70

The structure of the complex and the formation of the products from it are given below:

$$C_6H_5CH - O - C_6H_4 - X$$

$$H \quad\quad Cl \quad\quad\quad\longrightarrow\quad\quad C_6H_5CH = O^+ C_6H_4 - X$$

$$Cl$$

A similar complex is given by Deno and Potter [38] in the study of oxidative cleavage of ethers by aqueous bromine. The synchronous electron pair loss and H^+ loss has been proposed by Westheimer [39] for the oxidation of alcohols by chromic acid.

$$C_6H_5CH = O^+ C_6H_4 - X + H_2O \longrightarrow \begin{Bmatrix} C_6H_5CH\ OC_6H_4 - X \\ | \\ O^+H_2 \end{Bmatrix}$$

$$C_6H_5\underset{\underset{O}{\parallel}}{C}\ OC_6H_4 - X \quad + \quad 3H^+$$

{X = H, *o*-Me, *m*-Me, *p*- Me, *o*-Cl and *p*-NO$_2$, }

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In the presence of water, this intermediate is converted in to the corresponding benzoates. A similar type of hydrolysis is reported in the electrochemical oxidation [40] of benzyl ethers to benzoates and in the oxidation of benzyl ethers with sodium hypochlorite mediated by N-Oxoammonium salt [41].

Table-2: Rate constants for the oxidation of benzyl phenyl ethers by NCS and Activation Parameters

[Substrate] = 2.0×10^{-2} M   [NCS]   = 3.0×10^{-3} M
[NaClO$_4$] = 1.0×10^{-1} M   Solvent (v/v) = 80% CH_3COOH -20% H_2O
[HCl]   = 1.0×10^{-1} M

Substrate	$k_{obs} \times 10^4$ s^{-1}				E_a kJ mol^{-1}	$\Delta H^{\#}$ kJ mol^{-1}	$\Delta S^{\#}$ JK^{-1} mol^{-1}	$\Delta G^{\#}$ kJ mol^{-1}
	313 K	318 K	323 K	328 K				
Benzyl phenyl ether	9.82	11.51	15.03	18.56	35.53	32.89	-86.19	60.30
Benzyl o-methylphenyl ether	9.32	11.63	14.01	17.28	33.89	31.25	-88.32	59.33
Benzyl m-methylphenyl ether	10.02	12.05	14.43	17.72	30.65	28.01	-92.62	57.46
Benzyl p-methylphenyl ether	8.10	10.17	12.98	16.12	38.39	35.75	-82.66	62.03
Benzyl o-chlorophenyl ether	9.32	11.39	14.77	18.04	37.26	34.62	-83.79	61.26
Benzyl p-nitrophenyl ether	9.89	11.89	14.28	17.97	34.73	32.09	-87.09	59.78

REFERENCES

[1] Yong-Hak Kim; Karl-Heinrich Engesser. *Appl. Environ. Microbiol.,* **2004**, 70(7), 4398

[2] CA Godfrey; BM Trost; I Flemming. *Comprehensive Organic Synthesis*, **1991**, 7, 235

[3] PF Schuda; Cichowicz; MR Heimann. *Tetrahedron Lett.,* **1983**, 24, 3829

[4] BS Bal; KD Kochhar; HW Pinnick, *J. Org. Chem.,* **1981**, 46, 1492

[5] HJ Schmidt; HJ Schajer, *Int. Ed. Engl.,* **1979**, 18, 69

[6] EC Juenge; DA Beal, *Tetrahedron Lett.,* **1968**, 5819

[7] P Angibeaud; A Defaye; Gadelle; JP Utille, *Synthesis,* **1985,** 1123

[8] M Sasidharan; S Suresh; Sudalai., *Tetrahedron Lett.,* **1995,** 36, 9071

[9] SR Joshi; SB Sawant; JB Joshi, *Organic Process Research and Development,* **2001**, 5, 152

[10] M Balasubramaniyam; V Priya; N Mathiyalagan, *J. Indian Chem. Soc.,* **2010**, 87, 967

_____

[11] V Priya; N Mathiyalagan; John Bosco , *J. Indian Chem. Soc.*, **2009**, 86, 453

[12] N Mathiyalagan; R Sridharan, *J. Indian Chem. Soc.*, **2006**, 83, 434

[13] S Abdelrahman; Mayhoub; Arindam Talukdar; Mark Cushman, *J. Org. Chem.,* **2010**, 75, 3507

[14] Cooper; Terence Albert; William, *J. Chem. Soc.*, **1967**, 5, 455

[15] Yoshiro Ogata; Yasuhiko Sawaki, *J. Am. Chem. Soc.*, **1966**, 88, 5832

[16] N Kathryn Ranki; J Jennifer Henry, *J. Chem. Soc.*, **1998**, 39, 1095

[17] Wuyi Wang; Tiecyhaoli; Giorgion Attardo, *J. Org. Chem.*, **1997**, 62(19), 6598

[18] SA Grabovskiy; QK Timerghazin, *Russian Chemical Bulletin*, **2002**, 54, 2384

[19] A Jagathesan; K Nambi; SJ Arulraj, *Indian J. Chem.*, **1984**, 28A, 904

[20] R Filler, *Chem. Rev.*, **1963**, 63, 21

[21] W Marek Golebiewski; Miroslaw Gucma, Thieme *e Journals Synthesis*, **2007**, 23, 3599

[22] Banerji K Kalyan , *J. Chem. Soc.*, **1988**, 6, 1015

[23] N Nirmala Halligudi; M Desai; T Nandibewoor; Sharanappa, *Oxid. Commun.*, **2000,** 23(1), 117

[24] N Nirmala Halligudi; M Desai; T Nandibewoor T, *Indian J. Chem.*, **1999**, 38A, 943

[25] MS Ramachandran; R Santhanalakshmi; D Easwaramoorthy, *Oxid. Commun.*, **1998**, 21(2), 230.

[26] Jacques Einhorn; Cathy Einhorn; Fabien Ratajczak; Jean Louis Pierre, *J. Org. Chem.*, **1996**, 61(21), 7452

[27] N Mathiyalagan; R Sridharan, *Indian J. Chem.,* **2005**, 44A(10), 2044

[28] NN Halligudi; S Desai, *Oxid. Commun.*, **2004**, 27(2), 307

[29] Yanqing Peng; Gonghua Song, *The Royal Society of Chemistry,* **2002**, 4, 349

[30] S Venkateswaralu; V Jagannadham, *Indian J. Chem.*, **1988**, 27A, 314

[31] N Mathiyalagan; R Sridharan; V Priya, *J. Indian Chem. Soc.*, **2005**, 82, 795

[32] S Khan; MU Khan, SK Singh; HD Gupta; PK Singh, *Asian J. Chem.*, **2003**, 15, 595

[33] MD Carr; BD England, *Proc. chem. Soc*, **1958**, 350

[34] RE Pearson; JC Martin, *J Am Chem Soc*, **1963**, 85, 354

[35] NS Srinivasan; N Venkatasubramanian, *Tetrahedron Lett*, **1970**, 24, 2039

[36] NS Srinivasan; N Venkatasubramanian, *Tetrahedron,* **1970**, 30, 419.

[37] K Vivekanandan; K Nambi, *J Indian Chem. Soc*, **1999**, 76, 198

[38] NC Deno; Neil.H.Potter, *J. Am. Chem. Soc.,* **1967**, 89**,** 3550.

[39] F Westhemier, *J. Am. Chem. Soc.*, **1960**, 82, 406.

[40] JW Boyd; PW Schmalzl; LL Miller, *J Am Chem. Soc.*, **1980**, 102, 3856.

[41] Nam Sook Cho; Chan Hean Park, *Bull. Korean Chem. Soc.,* **1994**, 15(11), 924.