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A KINETIC AND MECHANISTIC STUDY OF OXIDATION OF BENZYL *m*-METHYL PHENYL ETHERS BY USING N-CHLORO SUCCINIMIDE

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Abstract

This paper reports the kinetic and mechanistic study of oxidation of Benzyl *m*-Methyl phenyl ethers by using N-Chloro Succinimide, The Effect of various process parameters such as Cation removal and chelating formation and structure has been studied for the Experimental data of product molecules and characteristic parameters were analyzed by FT-IR, Velocity measurement and Polymerization test.

Keywords: kinetic and mechanistic study, Benzyl *m*-Methyl phenyl ethers, FT-IR.

INTRODUCTION

N-Halogeno compounds are known to be versatile oxidizing agents. N-halo reagents are widely used in fine organic synthesis and in the chemistry of natural compounds. And also the role of N-halo compounds in the field of kinetics is very wide. Many N-halo compounds are used as important reagents in organic chemistry. These include N-halo amides, N-halo carbamates, N-halo ureas and so on.

The N-halo compounds such as N-chloro Succinimide, N-chlorophthalimide, N-chloroamines, N-chlorocaprolactam, N-chlorobenzamide, N-chlorosaccharin, N-chloropiperidone have already been used in the oxidation reactions. The study of kinetics involving N-halo compounds has led to the mechanism of their action.

Some specific features of N-halo Succinimide determine their wide application in organic synthesis. N-halo Succinimide are sources of positive halogens and these reagents have been exploited as oxidants for a variety of substrate. This is due to the high liability 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 Succinimide promote very important reactions, such as halogenations, Solvolytic halogenations, oxidation, as well as other processes resulting in formation of compounds with C-X, C-O, C=O, S-X, P-X, C-N, P-N, S-N, S=N, etc...

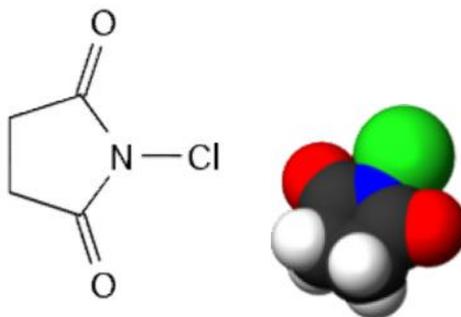
The application of N-halo reagents (such as N-halo amines, N-halo amides and/or imides, N-halo sulfonamides and/or imides, and *etc.*) are reported in various organic functional group transformations such as: oxidation reactions, deportation and protection of different functional groups, halogenations of saturated and unsaturated compounds, acylation of alcohols, phenols, amines or thiols, epoxidation of alkenes, aziridination *etc.*,

Literature survey shows that there does not seem to be an up-to-date review articles on the kinetics studies of N-chlorosuccinimide oxidation of benzyl phenyl ethers. Hence a general review of work done on oxidation of benzyl *m*-Methyl phenyl ethers with other oxidants and kinetic studies on oxidation with N-Chloro Succinimide is given in this chapter as a background for the present investigation.

N- CHLORO SUCCINIMIDE:

N-Chloro Succinimide (NCS) is a versatile reagent and its significance is not limited to chlorination and oxidation⁷. 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, and formation of new carbon-carbon bonds,

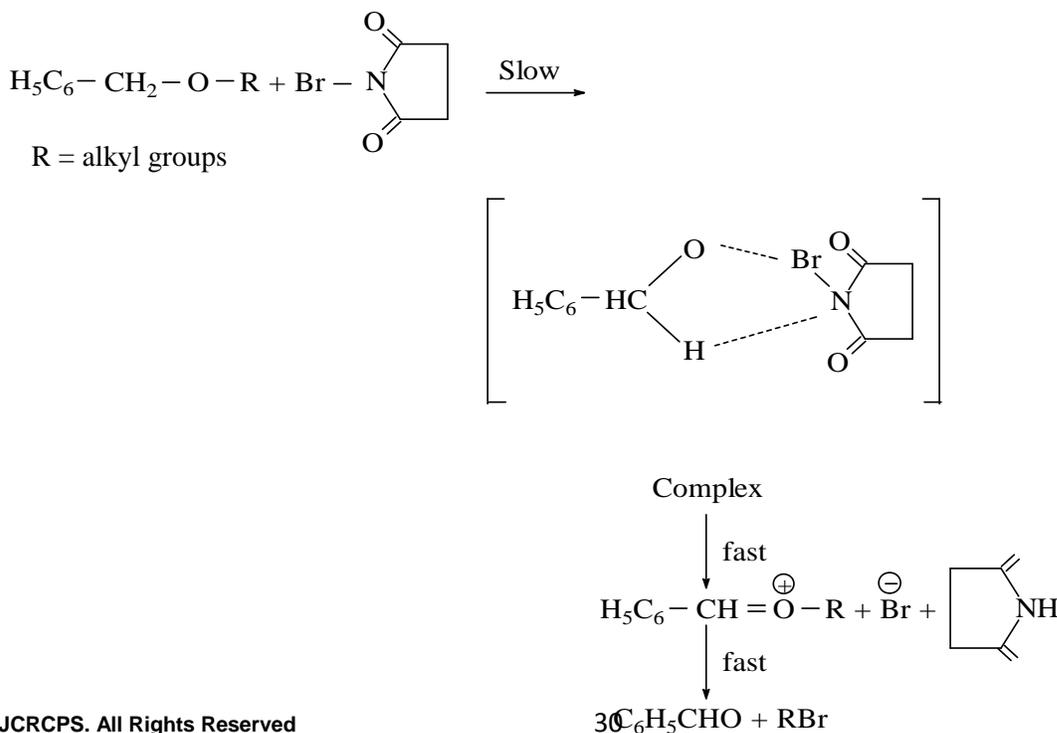
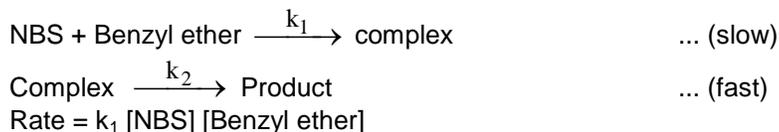
rearrangements, and functional group transformations. It can be used as pharmaceutical intermediates, organic synthesis chlorinating agent. It can also be used to prepare rubber additives, antibiotic drug intermediates. N-Chloro Succinimide is also used as an intermediate or a chlorinating agent in the synthesis of pharmaceuticals especially for tetracycline antibiotics.

**OXIDATION OF BENZYL ETHERS BY N-BROMOSUCCINIMIDE:**

Kinetics of oxidation of benzyl ethers by N-Bromo Succinimide (NBS) in 80% aqueous acetic acid had been reported³¹. Here the reaction followed first order kinetics with respect to both [NBS] and [substrate].

The effect of varying ionic strength and dielectric constant indicated that the reaction was a dipole-dipole type. The product of oxidation was found to be Benzaldehyde

The mechanism proposed for the oxidation of benzyl ether by NBS.



MATERIALS AND METHODS

REAGENTS

ACETIC ACID:

500 ml of ordinary glacial acetic acid was taken in a one liter round bottomed flask. 20 g of solid chromium tri-oxide was added. The flask was refluxed in water condenser for about four hours. It was then cooled and distilled. Pure acetic acid was collected at 118°C and stored in closed brown bottles.

PHENOLS:

Phenol, m-methyl phenol, p-nitro phenol were purified by the standard method.

BENZYL CHLORIDE:

Benzyl chloride was used as such.

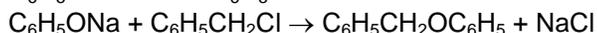
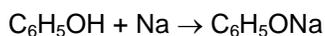
OXIDANT

Commercial sample of N-Chloro Succinimide was used as such.

PREPARATION OF BENZYL PHENYL ETHERS

Benzyl phenyl ether

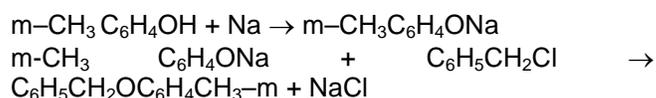
About 43.9ml of distilled phenol was taken in a round bottomed flask and a piece of calculated amount of metallic sodium was added till the maximum amount was dissolved. The sodium phenoxide formed was cooled. Required quantity of distilled benzyl chloride should be added. Benzyl chloride reacts with sodium phenoxide to form benzyl phenyl ether and sodium chloride.



The flask was cooled and the contents were poured into excess of water. The sodium chloride dissolves in excess of water and benzyl o-methyl phenyl ether was separated by using the separating funnel. It was washed well with distilled water and distilled under vacuum (or) low pressure distillation.

Benzyl m-methyl phenyl ether

About 52.3ml of distilled m-methyl phenol was taken in a round bottomed flask and a piece of calculated amount of metallic sodium was added till the maximum amount was dissolved. The sodium m-methyl phenoxide formed was cooled. Required quantity of distilled benzyl chloride should be added. Benzyl chloride reacts with sodium phenoxide to form benzyl m-methyl phenyl ether and sodium chloride.

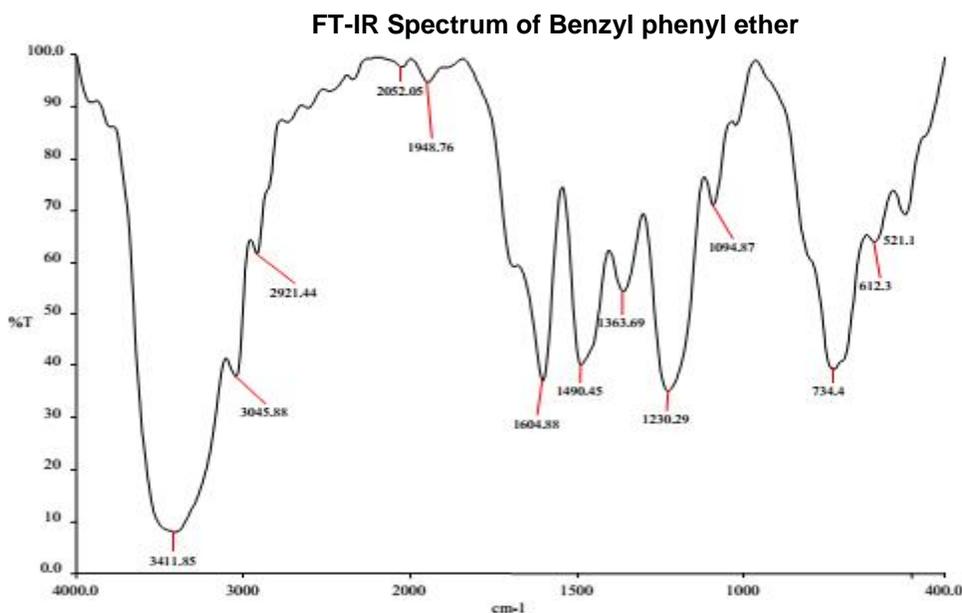


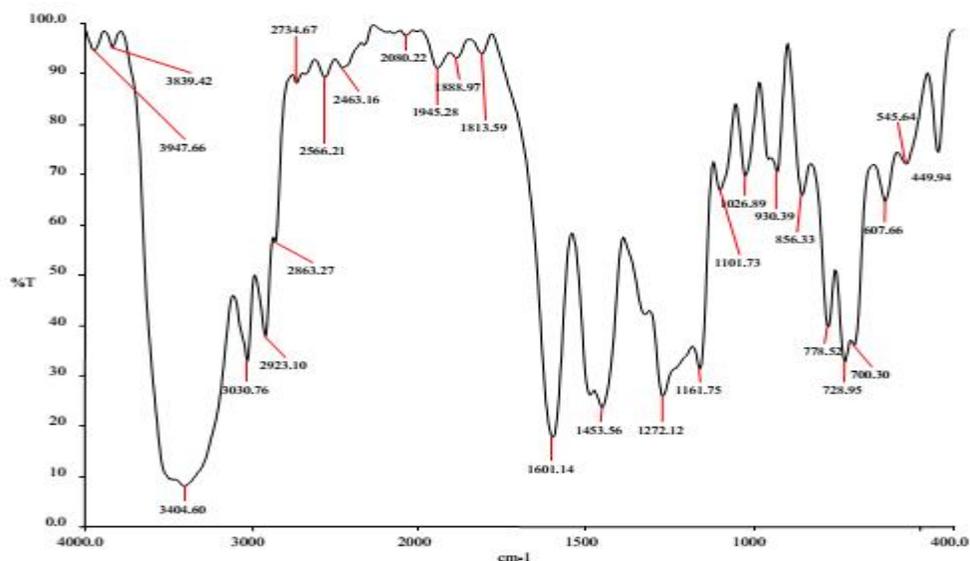
The flask was cooled and the contents were poured into excess of water. The sodium chloride dissolves in excess of water and benzyl m-methyl phenyl ether was separated by using the separating funnel. It was washed well with distilled water and distilled under vacuum (or) low pressure distillation.

Physical measurements

Infrared Spectra

The infrared spectra of all the complexes were recorded on a Perkin Elmer FT-IR Spectrometer in the range of 4000 – 400 cm⁻¹ using KBr pellets.





KINETIC METHODS

Preparation of standard solution:

The standard stock solution of NCS was prepared by dissolving the required quantity of it in water and standardized by titrating against standard sodium thiosulphate solution iodometrically. This NCS solution was found to be invariant in its strength over a period of three months. The benzyl phenyl ether solutions were prepared by dissolving required quantity of them in acetic acid and water mixture (v/v).

Velocity measurement

In a typical experiment, the required quantities of the benzyl phenyl ether solution, hydrochloric acid, sodium per chlorate and acetic acid – water mixture were pipetted out in a clean dried reaction bottle, kept in thermostat, set at the desired temperature. The reaction was started by pipetting out the required quantity of NCS solution, which had also been thermo stated for nearly half an hour. The total volume of the reaction mixture was always 25 ml. 3ml of reaction mixture was pipetted out into the conical flask and the progress of the reaction was followed iodometrically.

Investigation of stoichiometry:

The stoichiometry of the reaction [NCS]:[benzyl phenyl ethers] was determined by taking excess of NCS over the substrate and the allowing the reaction for completion since the concentration of the benzyl phenyl ethers taken was less compared to that of NCS, all the benzyl phenyl ethers taken would have been completely reacted leaving behind the unreacted NCS, the concentration of which was estimated by iodometry. Estimation of unreacted NCS showed that

one mole of benzyl phenyl ethers consumed two moles of NCS.

Product study:

For product study, the substrate was taken in excess compared to concentration of oxidant. The reaction mixture was kept aside for about 48 hours for the completion of the reaction. After that the residual mixture was poured into a separating funnel. Solvent ether was added and shaken well. Then it was washed with distilled water and the ether layer was separated, dried with anhydrous sodium sulphate. After washing several times with water, it was dried and the product was analyzed. The major product was found to be Benzaldehyde. It was confirmed by TLC.

Polymerization test:

Addition of definite concentration of methyl methacrylate solution to the reaction mixture did not affect the rate of the reaction, which indicates the non-involvement of the free radical intermediate during the oxidation of benzyl phenyl ether by NCS.

Thermodynamic parameters

In kinetics, the variation of reaction rate with temperature is usually expressed by the Arrhenius equation, which in its integrated form is

$$\log k = \log A - \frac{E_a}{2.303 RT}$$

Where,

k - is the rate constant at temperature T
A - is the pre-exponential factor
E_a - is the Arrhenius activation energy
R - is the universal gas constant

This equation is in accord with the experimental fact that for the most of the reactions, a plot of $\log k$ versus $1/T$ is a straight line.

The slope of the line is $-E_a / 2.303 R$; E_a calculated in this way is known as the Arrhenius activation energy. From the calculated E_a , the other thermodynamic parameters are calculated using the following expressions.

$$k = Ae^{-E_a/RT}$$

The enthalpy of activation ΔH^\ddagger can be calculated from the equation

$$\Delta H^\ddagger = E_a - RT$$

The free energy of activation ΔG^\ddagger is given by

$$\Delta G^\ddagger = \Delta H^\ddagger - T\Delta S^\ddagger$$

The entropy of activation ΔS^\ddagger is given by Eyring equation

$$A = \frac{k_B T}{h} e^{\Delta S^\ddagger / R}$$

$$k = \frac{k_B T}{h} \times e^{\Delta S^\ddagger / R} \times e^{-\Delta H^\ddagger / RT}$$

Where

A	–	Pre exponential factor
ΔH^\ddagger	–	Enthalpy of activation
ΔS^\ddagger	–	Entropy of activation
ΔG^\ddagger	–	Free energy of activation
K_b	–	Boltzmann constant
h	–	Plank's constant

RESULT AND DISCUSSION

In the present study, a series of benzyl phenyl ethers have been chosen to study the kinetics and mechanism of oxidation by NCS. Benzaldehyde is the major product of oxidation. The rates of the reaction were measured by following the disappearance of NCS iodometrically in acetic acid medium. The kinetic study of oxidation had been carried out in the presence of HCl and NaClO_4 .

OXIDATION OF BENZYL PHENYL ETHER WITH NCS:

Order of Reaction With Respect to NCS:

A plot of $\log [\text{NCS}]$ Vs time is linear indicating first-order dependence on $[\text{NCS}]$ [Fig.1]. A typical kinetic run has been shown in **TABLE 1**

A typical kinetic run for the NCS oxidation of benzyl methyl ether

[Benzyl phenyl ether]= 2×10^{-2} M	[NCS]= 3×10^{-3} M
Solvent=80% CH_3COOH (v/v)	[HCl]=0.1M
[NaClO_4]= 0.1M	Temperature=318K

Time in seconds	$\log[\text{NCS}]$, where $[\text{NCS}] = a - x$
300	0.7993
600	0.6532
900	0.5052
1200	0.3802
1500	0.2041
1800	0.0414

Effect of variation of NCS Concentration:

The oxidation was carried out with different initial Concentrations of NCS and the results are given in Table 2.

TABLE 2 Effect of concentration of NCS on the reaction rate

[Benzyl phenyl ether]= 2×10^{-2} M	[HCl]=0.1M
Solvent=80% CH_3COOH (v/v)	[NaClO_4]= 0.1M
Temperature=318K	

$[\text{NCS}] \times 10^3 \text{ M}$	$K_{\text{obs}} \times 10^4 \text{ s}^{-1}$
2.0	8.21
3.0	11.51
4.0	13.43
5.0	14.97
6.0	17.27
7.0	19.20

It is seen that the pseudo first-order rate constant increases with increase in the initial concentration of the oxidant. But in each kinetic run, the reaction shows no deviation from the first order plot of $\log [\text{NCS}]$ Vs time.

The values of the rate constants of other benzyl phenyl ethers also increase with increase in initial concentration of NCS. However it must be stressed that the reaction follows first-order with respect to oxidant at every one of these concentrations.

Order with respect to substrate:

Effect of Variation of Benzyl Phenyl Ether Concentration:

The rate of oxidation was carried out with different initial concentration of benzyl phenyl ether and keeping the $[\text{NCS}]$ as constant (Table 3). The rate of the reaction remains constant with increase in the concentration of the substrate. It is found that the reaction follows zero order kinetics with respect to substrate.

TABLE 3 Variation k_{obs} with Benzyl phenyl ether

$[\text{NCS}] = 3 \times 10^{-3} \text{M}$ $[\text{HCl}] = 0.1 \text{M}$
 Solvent = 80% CH_3COOH (v/v) $[\text{NaClO}_4] = 0.1 \text{M}$
 Temperature = 318K

$[\text{BPE}] \times 10^2 \text{M}$	$K_{\text{obs}} \times 10^4 \text{s}^{-1}$
1.0	11.43
2.0	11.51
3.0	11.20
4.0	11.43
5.0	12.08
6.0	11.56

Effect of Succinimide on Reaction Rate:

The effect of Succinimide on reaction rate was studied by adding different amounts of Succinimide, keeping

the concentration of benzyl phenyl ether and NCS constant. The rate of the reaction remains constant with the increase in the initially added amount of Succinimide

TABLE 4 Variation of k_{obs} with added Succinimide

$[\text{Benzyl phenyl ether}] = 2 \times 10^{-2} \text{M}$ $[\text{NCS}] = 3 \times 10^{-3} \text{M}$
 Solvent = 80% CH_3COOH (v/v) $[\text{HCl}] = 0.1 \text{M}$
 $[\text{NaClO}_4] = 0.1 \text{M}$ Temperature = 318K

$[\text{NH}] \times 10^3 \text{M}$	$K_{\text{obs}} \times 10^4 \text{s}^{-1}$
1.0	10.21
2.0	10.47
3.0	10.55
4.0	10.07
5.0	10.13
6.0	10.27

Effect of variation of HCl concentration:

The influence of variation of acid concentration on the reaction rate was studied by varying the concentration of added hydrochloric acid at constant [benzyl phenyl

ether] and $[\text{NCS}]$ (Table 4). In all these cases, the reaction rate increases with the increase in $[\text{HCl}]$. The plot of $\log k_{\text{obs}}$ Vs $\log [\text{HCl}]$ is found to be linear with positive and unit slope

[Benzyl phenyl ether]= 2×10^{-2} M [NCS]= 3×10^{-3} M
Solvent=80% CH_3COOH (v/v) [NaClO₄]= 0.1M
Temperature=318K

[HCl]×10 M	$K_{obs} \times 10^4 \text{ s}^{-1}$
0.2	2.45
0.4	4.78
0.6	7.52
0.8	9.52
1.0	11.51
1.2	15.28
1.4	18.04
1.6	19.98

OXIDATION OF OTHER BENZYL PHENYL ETHERS BY NCS:

The oxidation of other Benzyl phenyl ethers, Benzyl m-methyl phenyl ether, Benzyl p-methyl phenyl ether has been studied for the purpose of comparison under pseudo-first order conditions in the presence of HCl, NaClO₄. All the benzyl phenyl ethers have been oxidized to Benzaldehyde by NCS.

The rate studies were conducted with variation in the initial concentration of NCS at constant substrate concentration. The results have been presented in Table 9. The data reveal a increase in the first order rate constants with an increase in the concentration of NCS.

The zero order dependence of the rate of various benzyl phenyl ethers is inferred from the observation that increases in ether concentration, the rate of oxidation remains constant.

The kinetics of the effect of variation of [HCl] on the NCS oxidation of benzyl Phenyl Ethers were studied. The results show a increase in the rate with increase in the concentration of hydrochloric acid

Kinetic runs were carried out for all the benzyl phenyl ethers to study the effect of solvent polarity on the rate of oxidation by NCS. The results shown that the rate of oxidation increases with increase in the percentage of acetic acid in the binary solvent mixture of acetic acid and water,. Plot of $\log k_{obs}$ Vs $1/D$ is linear with positive and unit slope for all benzyl phenyl ethers.

The effect of Succinimide on reaction rate was studied by adding different amounts of Succinimide for all the benzyl phenyl ethers. The data in Table 4 shows that the reaction rate is not altered significantly with the increase in the initially added amount of Succinimide.

CONCLUSION

Before suggesting a probable mechanism for the oxidation of benzyl phenyl ethers by NCS, the kinetic results of the present investigation are summed up as follows.

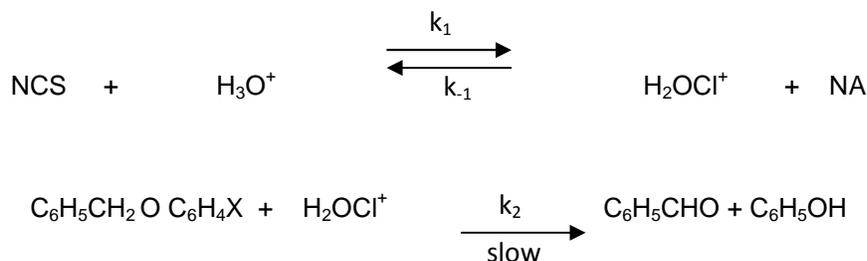
1. The reaction is first order with respect to the oxidant [NCS], and there is a increase in the values of the rate constants with increase in the initial concentration of the oxidant.
2. The reaction is zero order with respect to the [substrate], and the values of the rate constants remains constant with increase in the initial concentration of the substrate.
3. The rate of oxidation increases with the increase in the concentration of HCl.
4. The rate of the reaction is insensitive to change in NaClO₄ concentration.
5. Increase in the percentage of acetic acid in the binary solvent mixture of acetic acid and water increases the rate.
6. Increase in temperature increases the rate of the reaction and the plots of $\log k_{obs}$ Vs $1/T$ are linear for all the benzyl phenyl ethers. The entropy of activation is negative for all the benzyl phenyl ethers.
7. Initial addition of one of the products viz., nicotinamide, to the reaction mixture has a retarding effect on rate of oxidation.

Kinetic studies on NCS oxidation:

The active oxidizing species has to be identified, before suggesting a most probable mechanism. The possible oxidizing species under the experimental conditions are Cl₂, HOCl, H₂OCl⁺ and NCSH⁺ in aqueous solution. H₂OBr⁺ is the active oxidizing species in the oxidation of 4-Oxoacids by N-bromosuccinimide⁴⁴. In the oxidation of thiosemicarbazide⁴, maleic and crotonic acid⁴⁶ by N-Chloro Succinimide, H₂OCl⁺ is the active oxidant.

The rate of the reaction increases with the increase in $[H^+]$. Hence, it is presumed that H_2OCl^+ is the effective oxidizing species in the present investigation. This can fit in to all the experimental results for the oxidation of benzyl phenyl ethers by NCS. The first step is the interaction between NCS and aqueous H^+ , which

leads to the formation of the active oxidizing species. H_2OCl^+ interacts with the substrate in the slow step to give the products. The following mechanism is proposed for the oxidation of Benzyl phenyl ethers by NCS.



X = H, o-me, m-me, p-me, o-Cl, p-NO₂.

The rate law for the oxidation of benzyl phenyl ether by NCS is

$$\text{Rate} = k_2[\text{H}_2\text{OCl}^+][\text{substrate}]$$

Applying steady state approximation to the active oxidizing species,

$$\text{Rate} = \frac{k_2 k_1 [\text{NCS}] [\text{S}] [\text{H}_3\text{O}^+]}{k_{-1} [\text{NH}] + k_2 [\text{S}]}$$

Assuming $k_{-1}[\text{NH}] \ll k_2[\text{S}]$

$$\text{Rate} = k_1 [\text{NCS}] [\text{H}_3\text{O}^+]$$

The above rate law is consistent with the first order dependence of rate on $[\text{NCS}]$ and $[\text{H}^+]$.

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