

MECHANISTIC STUDY OF OXIDATION OF AROMATIC MONOETHERS BY N-HALO COMPOUND – A KINETIC APPROACH

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ABSTRACT

Three aromatic monoethers viz., benzyl methyl ether, benzylethyl ether, benzyl propyl ether are chosen for the mechanistic study of oxidation by N-chloronicotinamide (NCN) in aqueous acetic acid medium. The observed rate of oxidation is first order in [oxidant] and [HCl], zero order in [substrate]. An increase in the dielectric constant of the medium decreases the rate. Variation in ionic strength of the medium has no significant effect on the rate and the addition of the reaction product, nicotinamide has a slight retarding effect on the rate. The stoichiometry and product analysis have been carried out. From the effect of temperature on the reaction rate, the Arrhenius and thermodynamic activation parameters have been calculated. A suitable mechanism has been proposed and a rate law explaining the experimental results is obtained.

INTRODUCTION

N-chloronicotinamide [NCN] is an important N-halo compound. N-chloronicotinamide, the derivative of nicotinamide is a mild, stable, efficient and inexpensive oxidant for organic substrates vivekanandan et.al [1996]. The physical constants, stability in aqueous solution, the formal redox potential and elemental analysis confirms the presence of nitrogen-halogen bond. Hence the possibility of the compound serving as an effective source of positive halogen is established. Kinetic study of oxidation of tartaric acid L.pushpalatha et.al [2015], amino acids vivekanandan et.al [1999], aromatic aldehydes V.Ramasamy et.al [2006], alcohols N.Mathiyalagan et.al [2005], S-phenylmercaptoacetic acid K.Sathiyarayanan et.al [2006] by N-chloronicotinamide have been investigated.

Functionalization R.Filler [1963], at the α C-H bond of ethers is one of the most useful reactions in organic synthesis, because it provides way for the efficient preparation of esters. Benzyl ethers are commonly used as temporary protecting groups for alcohols, owing to the fact that they are stable to both acids and bases. Despite the numerous methods available for their cleavage, which include catalytic and chemical hydrogenolysis, transfer hydrogenation, bromination hydrolysis, acetolysis and the use of halosilane reagents or Lewis acid-thiol systems, problems associated with reagent incompatibility or slow debenzylolation rates often arise when multiple functionality is present. Kinetic study of oxidation of aromatic ethers by some N-halo compounds like, 1-chlorobenzotriazole M.Fieser et.al [1967], and N-bromonicotinamide J.Anil kumar et.al [2007] have been investigated.

EXPERIMENTAL

Glacial acetic acid (Merck, unaffected by chromic acid GR) was used as a solvent for benzyl ethers, which were prepared by Williamson's synthesis. Benzyl ethers, after isolation were then characterized by boiling point. Final characterization of benzyl ethers was carried out using IR (Spectrum RX1, Perkin Elmer) and $^1\text{H-NMR}$ spectra (Bruker). The IR spectrum of benzyl ethers showed characteristic absorptions for $\text{C}=\text{O}$ in the region $1020\text{-}1200\text{ cm}^{-1}$. The oxidant, N-chloronicotinamide was prepared by the chlorination of nicotinamide. The melting point was $221\text{ }^\circ\text{C}$. NCN was characterized by $^1\text{H-NMR}$ spectra.

Benzyl ether solution was prepared by dissolving required quantity of it in acetic acid-water mixture (v/v). The standard stock solution of NCN was prepared by dissolving the required quantity of it in water and standardized by titrating against standard sodium thiosulphate solution iodometrically. In a typical experiment, the required quantities of the benzyl ether solution, hydrochloric acid, sodium perchlorate

and acetic acid – water mixture were pipetted out in a clean dried reaction bottle, kept in thermostat for about half an hour, set at the desired temperature. The reaction was started by pipetting out the required quantity of NCN solution, which had also been thermostated for nearly half an hour. The total volume of the reaction mixture was always 25 ml. About 3 ml of reaction mixture was pipetted out into the conical flask and the progress of the reaction was followed iodometrically. All the experiments were carried out under pseudo-first order conditions with substrate concentration in excess. The pseudo-first order rate constants $[k_1]$ were obtained graphically by plotting $\log [\text{oxidant}]$ vs time.

The stoichiometry of the reaction was determined by taking excess of $[\text{NCN}]$ over benzyl ether], which was found to be 1:1.

In a typical experiment, a mixture of benzyl alkyl ether (0.04 M), NCN (0.02 M) was made upto 50 ml with water-acetic acid mixture [1:4] in the presence of HCl [0.1 M] and $\text{NaClO}_4 \cdot \text{H}_2\text{O}$ [0.1M]. The mixture was thermostated for 1 h to ensure the completion of the reaction. Then the solution was diluted with water and excess NCN was carefully removed with sodium thiosulphate solution. The residual mixture was then extracted with ether and washed with water. The organic layer was separated and dried over anhydrous sodium sulphate. The solvent was removed under reduced pressure. A careful TLC [silica gel] analysis of the mixture using benzene as the developing medium indicated the presence of benzaldehyde. Formation of benzaldehyde was also confirmed by the addition of 2,4-dinitrophenyl hydrazine. The aldehyde was converted to 2,4-dinitrophenyl hydrazone. The melting point of 2,4-DNP derivative is 253 °C [lit. m.p. 248 °C]. The identity of the product was further confirmed by $^1\text{H-NMR}$ spectrum

RESULTS AND DISCUSSION

The kinetics of oxidation of aromatic monoethers by NCN have been investigated at several initial concentrations of the reactants. Under the condition $[\text{NCN}] \ll [\text{substrate}]$, the oxidation proceeds smoothly at 45°C in aqueous acetic acid medium and the plots of $\log [\text{NCN}]$ vs time are found to be linear over 50% completion of the reaction, which shows the first order dependence of rate on $[\text{NCN}]$. The rate studies have been carried out with variation in the initial concentrations of NCN at constant concentration of aromatic monoethers. The constancy in the values of k_1 also confirms the first order dependence [Table 1] of rate on $[\text{NCN}]$.

Table 1: Effect of variation of $[\text{NCN}]$ for the oxidation of benzyl alkyl ethers at 318 K

$[\text{C}_6\text{H}_5\text{CH}_2\text{-O-R}] = 2.0 \times 10^{-2}\text{M}$ $[\text{HCl}] = 1.0 \times 10^{-1}\text{M}$
 Solvent (v/v) = 80% CH_3COOH – 20% H_2O $[\text{NaClO}_4 \cdot \text{H}_2\text{O}] = 1.0 \times 10^{-1}\text{M}$

$[\text{NCN}] \times 10^3(\text{M})$	$k_1 \times 10^4(\text{s}^{-1})$		
	R=methyl	R=ethyl	R=propyl
1.0	4.38	4.15	3.96
2.0	4.38	4.03	3.85
3.0	4.16	4.05	3.51
4.0	4.12	4.32	3.63
5.0	4.25	4.33	3.83

The dependence of rate on substrate concentration has been determined by measuring the first order rate constants for NCN disappearance over a wide range of substrate concentration at 45°C. The constancy of pseudo-first order rate constant at different $[\text{substrate}]$ shows that the reaction is zero order [Table 2] in $[\text{substrate}]$.

Table 2: Effect of variation of $[\text{benzyl alkyl ether}]$ for the oxidation by NCN at 318 K

$[\text{NCN}] = 3.0 \times 10^{-3}\text{M}$ $[\text{HCl}] = 1.0 \times 10^{-1}\text{M}$
 Solvent (v/v) = 80% CH_3COOH – 20% H_2O $[\text{NaClO}_4 \cdot \text{H}_2\text{O}] = 1.0 \times 10^{-1}\text{M}$

$[\text{C}_6\text{H}_5\text{CH}_2\text{-O-R}] \times 10^2(\text{M})$	$k_1 \times 10^4(\text{s}^{-1})$		
	R=methyl	R=ethyl	R=propyl
1.0	3.85	4.10	3.68
2.0	4.16	4.05	3.51
3.0	4.40	4.57	3.47
4.0	4.60	4.35	3.60
5.0	3.95	3.92	3.52

In order to study the effect of [HCl] on the reaction, the concentration of HCl has been varied in the range 0.05 – 0.25 M. The pseudo-first order rate constant increases [Table 3] with the increase in [HCl].

Table 3: Effect of variation of [HCl] for the oxidation of benzyl alkyl ethers by NCN at 318 K

[C₆H₅CH₂-O-R] = 2.0 × 10⁻²M [NCN] = 3.0 × 10⁻³M
Solvent (v/v) = 80% CH₃COOH – 20% H₂O [NaClO₄.H₂O] = 1.0 × 10⁻¹M

[HCl] × 10 (M)	k ₁ × 10 ⁴ (s ⁻¹)		
	R=methyl	R=ethyl	R=propyl
0.5	1.95	1.78	1.65
1.0	4.16	4.05	3.51
1.5	5.67	5.92	4.81
2.0	7.94	8.02	6.65
2.5	9.08	10.10	8.53

The plots of log k₁ vs log [HCl] are linear with unit slopes indicating first order dependence of [HCl] on the rate of oxidation. The influence of solvent dielectric constant on the rate of NCN oxidation of aromatic monoethers has been studied in various solvent mixtures of acetic acid and water. The rate of oxidation increases [Table 4] on decreasing the dielectric constant of the medium. Plots of log k₁ vs 1/D, where D is the dielectric constant of the medium, give straight line with positive slopes.

Table 4: Effect of variation of dielectric constant for the oxidation of benzyl alkyl ethers by NCN at 318 K

[C₆H₅CH₂-O-R] = 2.0 × 10⁻²M [HCl] = 1.0 × 10⁻¹M
[NCN] = 3.0 × 10⁻³M [NaClO₄.H₂O] = 1.0 × 10⁻¹M

CH ₃ COOH-H ₂ O% (v/v)	D	k ₁ × 10 ⁴ (s ⁻¹)		
		R=methyl	R=ethyl	R=propyl
70 – 30	25.90	3.02	2.69	2.18
75 – 25	22.64	3.55	3.39	2.57
80 – 20	19.38	4.16	4.05	3.51
85 – 15	16.12	6.03	5.89	4.68
90 – 20	12.87	9.68	9.82	8.93

The reaction has been conducted at different ionic strengths using NaClO₄.H₂O by keeping the concentration of other reactants constant. Addition of NaClO₄.H₂O does not have much effect on the rate of reaction. The effect of one of the products of the reaction on the rate, has been studied by adding various concentrations of nicotinamide, keeping the concentrations of substrate and NCN constant. Addition of nicotinamide in the concentration range of 0.001 to 0.004 M has a negligible retarding effect. The oxidation of aromatic monoethers has been studied [Table 5] at four different temperatures [313 – 328 K].

Table 5: Effect of temperature on the rate of oxidation of benzyl alkyl ethers by NCN and evaluation of Arrhenius and thermodynamic activation parameters

[Ether] = 2.0 × 10⁻²M [HCl] = 1.0 × 10⁻¹M
[NCN] = 3.0 × 10⁻³M [NaClO₄.H₂O] = 1.0 × 10⁻¹M
Solvent (v/v) = 80% CH₃COOH – 20% H₂O

Substrate	k ₁ × 10 ⁴ (s ⁻¹)				E _a (kJ mol ⁻¹)	ΔG [‡] (kJ mol ⁻¹)	ΔH [‡] (kJ mol ⁻¹)	ΔS [‡] (J K ⁻¹ mol ⁻¹)	log A
	313 K	318 K	323 K	328 K					
Benzyl methyl ether	3.47	4.16	5.01	6.17	32.65	59.81	30.01	-93.72	1.98
Benzyl ethyl ether	3.16	4.05	4.79	6.16	37.04	62.33	34.04	-87.82	2.68
Benzyl n-propyl ether	2.56	3.51	4.57	6.02	48.31	68.86	45.67	-72.94	4.48

The temperature dependence on the rates of oxidation is determined by plotting log k₁ against reciprocal of temperature. The Arrhenius activation energy, pre-exponential factor, entropy, enthalpy and free energy of activation are evaluated.

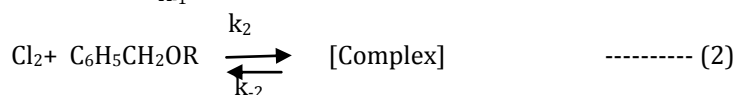
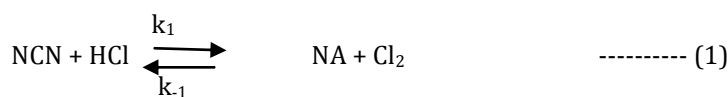
It has been observed that the rate of oxidation of aromatic monoethers is not altered by the initially added acrylonitrile, a typical radical trap. These observations indicate the absence of any free radical intermediate in the reaction.

Mechanism

The active oxidizing species has to be identified before any mechanistic interpretation should be advanced. In earlier studies with N-halo compounds in aqueous acid medium, Cl₂, HOCl, H₂OCl⁺, N,N-dichloronicotinamide and NCN in aqueous solution itself are discussed S.C.Negi et.al [1982] to be the probable reactive species. If NCNH⁺ 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. A simultaneous attack of H⁺ and Cl[⊖] ion on the N-haloamide leading to the release of molecular chlorine has been suggested.

Addition of nicotinamide [NA] decreases the rate of oxidation. This retarding effect suggest that the pre-equilibrium step involves a process in which nicotinamide [NA] is one of the products. If this equilibrium is involved in the oxidation process, the rate should be an inverse function of nicotinamide concentration, which is in agreement with the experimental observation.

Taking into consideration the set of kinetic data presented and the evidence for the formation of reactive molecular chlorine in the course of the reaction, the following mechanism may be proposed.



R = methyl, ethyl and propyl

This mechanism leads to the rate law (4)

$$\frac{-d[\text{NCN}]}{dt} = k_3[\text{Complex}] \quad \text{----- (4)}$$

Applying steady-state approximation to the complex and the chlorine intermediates, the rate law assumes the form,

$$\text{Rate} = \frac{k_1 k_2 k_3 [\text{C}_6\text{H}_5\text{CH}_2\text{OR}] [\text{NCN}] [\text{HCl}]}{k_{-2} + k_3 \{k_{-1}[\text{NA}] + k_2[\text{C}_6\text{H}_5\text{CH}_2\text{OR}]\}} \quad \text{----- (5)}$$

The rate of the reaction decreases with the increase in [NA]. To account for this fact in the rate law, an assumption is made, where $k_{-1}[\text{NA}] \ll k_2[\text{C}_6\text{H}_5\text{CH}_2\text{OR}]$.

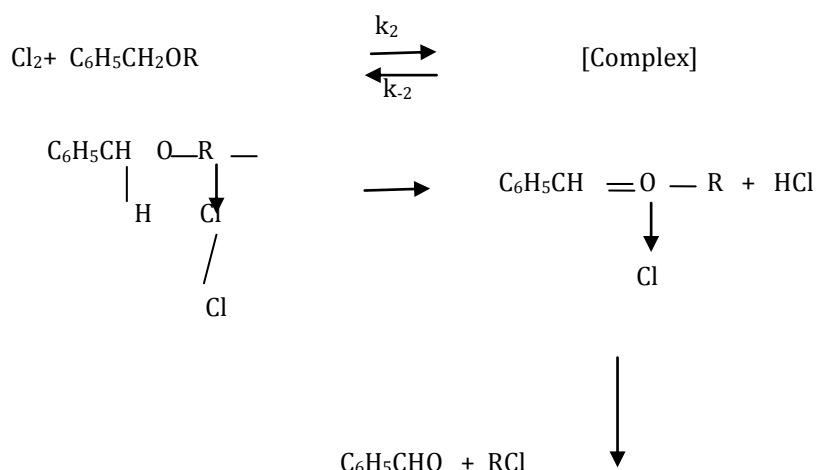
$$\text{Rate} = \frac{k_1 k_3 [\text{NCN}] [\text{HCl}]}{k_{-2} + k_3} \quad \text{----- (6)}$$

$$\text{Rate} = \frac{k_{\text{obs}} [\text{NCN}] [\text{HCl}]}{k_1 k_3} \quad \text{----- (7)}$$

$$\text{where } k_{\text{obs}} = \frac{k_1 k_3}{k_{-2} + k_3}$$

Equation [7] accounts for the first order dependence of rate on [NCN] and [HCl] and zero order dependence on [substrate].

The complex formed in the course of the reaction and the formation of the product may be represented in the following way:



The rate-determining step proposed in the above mechanism predicts negligible salt effect which has been experimentally observed. The positive values of the free energy of activation and the enthalpy of activation indicate that the transition state is highly ordered and the negative entropy of activation indicates the same.

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