

Kinetics and mechanism of oxidation of benzyl ethers by *N*-chloronicotinamide in aqueous acetic acid medium

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Abstract : Kinetics of oxidation of benzyl ethers by *N*-chloronicotinamide (NCN) in aqueous acetic acid medium have been investigated by potentiometric method. The observed rate of oxidation is first order in both [NCN] and [benzyl ethers]. An increase in the dielectric constant of the medium increases the rate. Addition of nicotinamide (NA), the reduction product of NCN, have a negligible effect on the rate of oxidation. A small increase in the rate is observed with increase in [HClO₄] and [NaCl]. Benzaldehyde is identified as the major product of oxidation.

Keywords : Oxidation, benzyl ethers, *N*-chloronicotinamide.

Introduction

N-Halo compounds are being used in kinetics, analytical¹, organic structural investigations and in synthesizing organic substances². *N*-Halo compounds are referred to as positive halogen compounds. *N*-Chloronicotinamide³ (NCN) is a new, mild, stable, efficient and inexpensive oxidant. Nicotinamide is a derivative of niacin (vitamin B³) with similar vitamin activity. Nicotinamide plays an important role in certain biochemical mechanisms in human cells. The derivative *N*-chloronicotinamide, the oxidant in the present study is prepared by the chlorination of nicotinamide. Hence the study becomes important from the biological point of view. An extensive literature survey reveals that kinetics and mechanism of oxidation of amino acids⁴, aldehydes⁵, alcohols^{6,7}, *S*-phenylmercapto acetic acid⁸ have been carried out using NCN. Ethers are widely used as solvents for a variety of organic compounds. The studies pertaining to the oxidation of ethers, especially benzyl ethers is very limited. Kinetic investigations involving oxidation of benzyl ethers by cobaltic salts⁹, nitric acid¹⁰ have been reported. Among the various *N*-halo compounds, only *N*-bromosuccinimide¹¹ has been used as effective oxidant for benzyl ethers. In continuation of this, the results of

the kinetic and mechanistic studies of the oxidation of benzyl ethers with NCN in aqueous acetic acid medium in the presence of perchloric acid and sodium chloride is reported.

Results and discussion

At constant [H⁺] with the [benzyl ether] in excess, the plot of log *E_t* (where *E_t* is the EMF of the cell at time *t*) vs time is linear, indicating first order dependence of rate on [NCN]. Increase in [benzyl ether] increases the rate of the reaction (Table 1). The plot of log *k_{obs}* vs log [benzyl ether] is linear with slope unity indicating first order dependence on [benzyl ether].

Table 1. Effect of [benzyl ethers] on the reaction rate at 328 K

[NCN] = 1.0 × 10⁻³ M, [HClO₄] = 0.1 M, [NaCl] = 0.1 M,
Solvent (v/v) = 80% CH₃COOH - 20% H₂O

[Benzyl ether] × 10 ² M	<i>k_{obs}</i> × 10 ³ (s ⁻¹)			
	Benzyl <i>n</i> -propyl ether	Benzyl <i>n</i> -butyl ether	Benzyl iso-propyl ether	Benzyl iso-butyl ether
1.0	5.19	8.82	12.16	14.31
2.0	10.41	17.61	24.34	28.65
3.0	15.36	26.46	36.45	42.91
4.0	20.51	35.22	48.60	57.17

The effect of $[H^+]$ is investigated by varying $[HClO_4]$ at constant $[Cl^-]$ and the rate remains constant with increasing acid strength (Table 2). The effect of Cl^- on the rate of the reaction is also studied by increasing $[NaCl]$ at constant $[HClO_4]$. It has been observed that the reaction rate remains constant with increase in $[Cl^-]$ (Table 3). Hence $NaCl$ act as inert salt, maintaining constant ionic strength.

Table 2. Effect of [perchloric acid] on the reaction rate at 328 K
 $[NCN] = 1.0 \times 10^{-3} M$, [benzyl ether] = $1.0 \times 10^{-2} M$, $[NaCl] = 0.1 M$, Solvent (v/v) = 80% CH_3COOH - 20% H_2O

$[HClO_4]$ $\times 10^2 M$	$k_{obs} \times 10^3 (s^{-1})$			
	Benzyl	Benzyl	Benzyl	Benzyl
	<i>n</i> -propyl ether	<i>n</i> -butyl ether	iso-propyl ether	iso-butyl ether
1.0	5.19	8.82	12.16	14.31
2.0	5.32	8.84	12.82	14.60
3.0	5.87	8.51	12.41	14.08
4.0	5.84	8.70	12.19	14.90

Table 3. Effect of [sodium chloride] on the reaction rate at 328 K
 $[NCN] = 1.0 \times 10^{-3} M$, [benzyl ether] = $1.0 \times 10^{-2} M$, $[HClO_4] = 0.1 M$, Solvent (v/v) = 80% CH_3COOH - 20% H_2O

$[NaCl]$ $\times M$	$k_{obs} \times 10^3 (s^{-1})$			
	Benzyl	Benzyl	Benzyl	Benzyl
	<i>n</i> -propyl ether	<i>n</i> -butyl ether	iso-propyl ether	iso-butyl ether
0.10	5.19	8.82	12.16	14.31
0.15	5.08	8.98	12.91	14.74
0.20	5.77	8.75	12.79	14.64
0.25	5.71	8.66	12.19	14.13

An increase in the rate constant is noticed on increasing the dielectric constant of the medium (Table 4). Plot of $\log k_{obs}$ vs $1/D$, where D is the dielectric constant of the medium, gives straight line with negative slope for different benzyl ethers, indicating the reaction is a dipole-dipole type.

Effect of added nicotinamide (NA) is studied at different initial concentrations of nicotinamide (Table 5). It has a negligible effect on the rate of oxidation.

The oxidation of all the benzyl ethers has been studied at different temperatures (323–338 K). The results are shown in Table 6. The Arrhenius plot of $\log k_2$ vs $1/T$ is linear. From the plot, the activation and thermodynamic parameters are evaluated (Table 7).

Table 4. Effect of varying solvent composition on the reaction rate at 328 K

[Benzyl ether] = $1.0 \times 10^{-2} M$, $[NCN] = 1.0 \times 10^{-3} M$, $[HClO_4] = 0.1 M$, $[NaCl] = 0.1 M$

$CH_3COOH-H_2O$ % (v/v)	D	$k_{obs} \times 10^3 (s^{-1})$			
		Benzyl <i>n</i> -propyl ether	Benzyl <i>n</i> -butyl ether	Benzyl iso-propyl ether	Benzyl iso-butyl ether
90–10	12.80	2.95	5.89	6.93	12.13
85–15	16.40	4.03	6.10	8.35	13.33
80–20	20.00	5.79	8.82	12.16	14.31
75–25	23.50	7.80	10.03	13.01	16.10
70–30	27.00	10.59	11.91	14.24	18.91

Table 5. Effect of [nicotinamide] on the reaction rate at 328 K

$[NCN] = 1.0 \times 10^{-3} M$, [benzyl ether] = $1.0 \times 10^{-2} M$, $[HClO_4] = 0.1 M$, Solvent (v/v) = 80% CH_3COOH - 20% H_2O , $[NaCl] = 0.1 M$

$[NA]$ $\times 10^3 M$	$k_{obs} \times 10^3 (s^{-1})$			
	Benzyl	Benzyl	Benzyl	Benzyl
	<i>n</i> -propyl ether	<i>n</i> -butyl ether	iso-propyl ether	iso-butyl ether
0.0	5.19	8.82	12.16	14.31
1.0	5.07	8.13	12.07	14.02
2.0	5.82	8.63	12.87	14.98
3.0	5.73	8.81	12.89	14.85
4.0	5.41	8.69	12.13	14.99

Table 6. Effect of temperature on the reaction rate

$[NCN] = 1.0 \times 10^{-3} M$, [benzyl ether] = $1.0 \times 10^{-2} M$, $[HClO_4] = 0.1 M$, Solvent (v/v) = 80% CH_3COOH - 20% H_2O , $[NaCl] = 0.1 M$

Temp. (K)	$k_2 \times 10 (dm^3 mol^{-1} s^{-1})$			
	Benzyl <i>n</i> -propyl ether	Benzyl <i>n</i> -butyl ether	Benzyl iso-propyl ether	Benzyl iso-butyl ether
323	2.72	4.67	6.67	7.98
328	5.19	8.82	12.16	14.31
333	9.70	16.31	21.76	25.24
338	17.82	29.65	38.28	43.71

Mechanism :

Under the experimental conditions studied Cl_2 , $HOCl$, $NCNH^+$ and NCN itself in aqueous solution can be the possible oxidizing species. The oxidation of amino acids by *N*-chlorobenzamide¹² and chlorobenzotriazole¹³ has been reported to take place through the intermediate forms

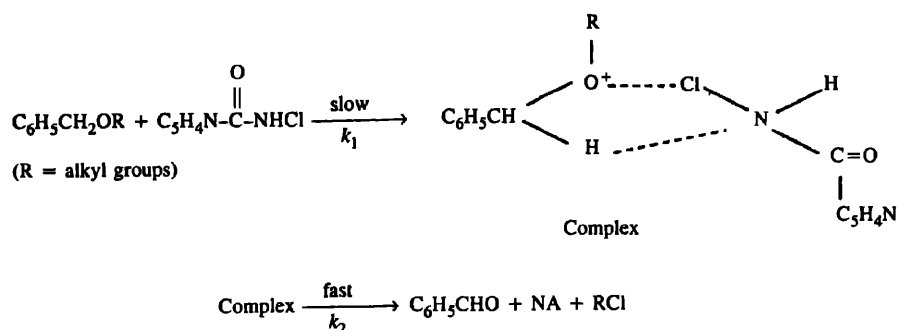
Table 7. Activation parameters for the oxidation of benzyl ethers at 328 K

Benzyl ethers	E_a (kJ mol ⁻¹)	$\ln A$	ΔH^\ddagger (kJ mol ⁻¹)	ΔG^\ddagger (kJ mol ⁻¹)	ΔS^\ddagger (JK ⁻¹ mol ⁻¹)
Benzyl <i>n</i> -propyl ether	113.65	19.81	110.96	98.73	37.84
Benzyl <i>n</i> -butyl ether	110.73	19.58	108.04	96.46	35.86
Benzyl iso-propyl ether	105.73	18.22	103.04	93.21	30.43
Benzyl iso-butyl ether	102.40	18.46	99.71	91.12	26.60

of protonated species of the oxidant or molecular chlorine. The oxidation of alcohols and aliphatic ketones by *N*-chlorosuccinimide¹⁴ and *N*-bromosuccinimide¹⁵ takes place through the protonated species NCSH^+ and NBSH^+ . In the present study, the rate does not increase much with increase in $[\text{HClO}_4]$. Hence the protonated form of the oxidant NCNH^+ cannot be the effective oxidizing species. A simultaneous attack of H^+ and Cl^- ion on the *N*-haloamide can lead to the release of molecular chlorine, as in the case of oxidation of amino acids⁴ by NCN . HOCl acts as the effective oxidizing species in the oxidation of aliphatic alcohols⁶ by NCN .

In the present investigation, the reaction is not catalyzed by H^+ and Cl^- , as the reaction rate does not increase much with the increase in $[\text{HClO}_4]$ and $[\text{NaCl}]$. Hence NCN itself can act as effective oxidizing species. Since the order with respect to NCN is unity, the possible oxidizing species is NCN itself. A similar *N*-halo compound, *N*-bromosuccinimide itself is shown to act an oxidizing species¹⁵⁻¹⁷ in aqueous acetic acid medium.

Taking into consideration the set of kinetic data presented above, the following mechanism may be proposed for the present oxidation study.



$$\text{Rate} = k_1 [\text{benzyl ether}] [\text{NCN}]$$

The first step is the interaction between benzyl ether and NCN which leads to the formation of a positively charged

complex. The positive part of oxidizing species viz. chlorine attacks the lone pair of oxygen of the ether in rate determining step. A similar mechanism has also been observed for the oxidation of benzyl ethers¹⁸ and alcohols¹⁹. The above mechanism also explains the first order behavior of oxidation with respect to $[\text{NCN}]$ and $[\text{benzyl ether}]$. The increase of rate with the increase in dielectric constant of the medium explains that the reaction is between two dipoles in rate determining step. The activation enthalpies and entropies of oxidation of all benzyl ethers are linearly related, implying that all the benzyl ethers undergo oxidation by the same mechanism.

Order of reactivity and isokinetic relationship :

The oxidation rates correlate well with Taft σ^* values²⁰ with negative value of reaction constant. The value of ρ^* at 323, 328, 333 and 338 K are -2.91, -2.63, -2.65 and -2.44 respectively. This indicates that the transition state of the reaction is positively charged. The negative value of reaction constant indicates that electron donating centers increase the rate of reaction. The reactivity order among the benzyl ethers is : benzyl iso-butyl ether > benzyl iso-propyl ether > benzyl *n*-butyl ether > benzyl *n*-propylether. The activation energy is the

highest for the slowest reaction. Such a reactivity order has been earlier reported in the oxidation of alcohols by

N-chloronicotinamide⁶ and oxidation of benzyl ethers by NBS¹¹. The order of reactivity is in accord with the inductive effects associated with the alkyl groups.

The genuine nature of isokinetic relationship was verified by the Exner plot^{21,22} of $\log k_2$ (328 K) vs $\log k_2$ (333 K) with slope 1.05. This linearity of Exner plot is suggestive of a unified mechanism for the NCN oxidation of different benzyl ethers. From the slope of the Exner plot, isokinetic temperature (β) is calculated using the following equation²³.

$$\beta = \frac{T_1 T_2 (b - 1)}{b T_2 - T_1}$$

The slope ' b ' is greater than 1 and β (252 K) is less than T_1 , which indicates an increasing selectivity with increase in temperature and the reaction series is characterized by compensation effect between ΔH^\ddagger and ΔS^\ddagger .

Experimental

Benzyl ethers viz. benzyl *n*-propyl ether, benzyl isopropyl ether, benzyl *n*-butyl ether and benzyl isobutyl ether were prepared from the corresponding alcohols and benzyl chloride by Williamson's synthesis. Standard solution of NCN was prepared in water and its purity was checked iodometrically.

Acetic acid (AnalaR, Qualigen) was purified by standard method²⁴. Perchloric acid (AnalaR) was used as a source of $[H^+]$. Conductivity water was used throughout the studies. Other chemicals used were of analytical grade. The kinetic runs were carried out under pseudo-first order conditions ($[benzyl\ ethers] \gg [NCN]$). Rate studies were carried out at the desired temperature with an accuracy of $\pm 0.5^\circ C$. The reaction was followed potentiometrically by setting up a cell consisting of a redox electrode (platinum wire was dipped in reaction mixture) and reference electrode (saturated calomel electrode). The EMF of the cell was measured periodically using Equip-Tronics digital potentiometer. The pseudo-first order constants were calculated from the plots of $\log E_t$ vs time.

Stoichiometry and product analysis :

The stoichiometry of the reaction was determined by taking excess of $[NCN]$ over $[benzyl\ ether]$. A mixture of benzyl ether (0.02 M), NCN (0.04 M), $HClO_4$ (0.1 M) and NaCl (0.1 M) was made up to 50 ml with water-acetic acid mixture (1 : 4). After the completion of the

reaction, the excess of NCN was determined iodometrically and several determinations with various benzyl ethers indicated 1 : 1 stoichiometry.

In a typical experiment, a mixture of benzyl ether (0.04 M), NCN (0.03 M) was made up to 50 ml with water-acetic acid mixture (1 : 4) in the presence of $HClO_4$ (0.1 M) and NaCl (0.1 M). The mixture was allowed to stand for 48 h to ensure the completion of the reaction. The residual mixture was then extracted with ether. The ether layer was separated and dried. Formation of benzaldehyde was 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 $253^\circ C$ (Lit. m.p. $248^\circ C$). The product was also confirmed by thin layer chromatography.

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