Mechanistic Study of Oxidation of Benzyl Ethers by 1-Chlorobenzotriazole in Glacial Acetic Acid

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In present studies, the kinetics of oxidation of benzyl ethers by 1-chlorobenzotriazole (CBT) in the presence of $HClO_4$ in aqueous acetic acid medium is reported. The observed rate of oxidation is first order with respect to [CBT] and [H^+]. The order with respect to [benzyl ether] is zero. The rate of the reaction increases with increase in the dielectric constant of the medium. Addition of benzotriazole has negligible effect on the rate of oxidation. The major product of oxidation is benzaldehyde. Arrhenius and activation parameters have been calculated. A suitable mechanism has been proposed and a rate law explaining the experimental results is derived.

Key Words: Kinetics, Oxidation, Benzyl ethers, Chlorobenzotriazole.

INTRODUCTION

1-Chlorobenzotriazole (CBT) has been extensively used in both chlorination and oxidation of many organic substrates. 1-Chlorobenzotriazole is one of the stable N-halo compounds[1] and is used as a source of electrophilic chlorine. It is a versatile oxidizing agent and its solution chemistry is reasonably well documented[2]. Kinetics of oxidation of chloramphenicol[3], dimethylamine[4], aromatic alcohols[5], fluoren-9-ols[6], mandelic acids[7], cyclohexanols[8], benzaldehyde[9], acetophenone oximes[10] and diazepam[11] by 1-chlorobenzotriazole are reported in the literature. There are a few reports on the kinetics of oxidation of medicinal compounds by 1-chlorobenzotriazole[11-13]. Prior investigations involving the oxidation of benzyl ethers did not yield a process of practical interest. Usually the amount of benzyl ether converted was too low to permit the process to be feasible commercially. Hence, an attempt has been made to study the oxidation of benzyl ethers at high temperature, so as to improve the yield of the product. The kinetics of oxidation of benzyl ethers[14,15], *p*-bromophenyl benzyl ether[16], substituted benzyl methyl ethers[17] by NBS is already known. However, the kinetics of oxidation of benzyl ethers by 1-chlorobenzotriazole is not reported so far.

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EXPERIMENTAL

Benzyl ethers, *viz.* benzyl *n*-propyl ether, benzyl *iso*-propyl ether, benzyl *n*-butyl ether, benzyl *iso*-butyl ether and benzyl *t*-butyl ether were prepared from the corresponding alcohols and benzyl chloride by Williamson's synthesis. 1-Chlorobenzotriazole was prepared from sodium hypochlorite and benzotriazole. Standard solution of 1-chlorobenzo-triazole was prepared in pure acetic acid and its purity was checked iodometrically. Acetic acid (AnalaR, BDH) was purified by standard method. Perchloric 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 ethers]>>[CBT]). Rate studies were carried out at a constant temperature. All the solutions were thermostated for 0.5 h before mixing. Requisite amounts of 1-chlorobenzotriazole in acetic acid, benzyl ether solution, perchloric acid 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 5 mL aliquot of the reaction mixture at various intervals of time and analyzing the oxidant concentration by quenching the solution in a mixture containing 2 mL of 5 % potassium iodide and 2 mL of 6 N sulphuric acid. The liberated iodine was titrated with a standard thiosulphate solution using starch as an indicator.

Stoichiometry and product analysis: The reaction mixture containing excess of 1-chlorobenzotriazole over benzyl ether in the presence of $HClO_4$ was kept at room temperature for 36 h. Estimation of unreacted 1-chlorobenzotriazole showed that one mole of benzyl ether reacted with one mole of 1-chlorobenzotriazole.

$$CBT + C_6H_5CH_2OR \longrightarrow Benzotriazole + C_6H_5CHO + RCl$$

For product study, the substrate was taken in excess compared to that of 1-chlorobenzotriazole. The reaction was allowed to proceed to completion by keeping it in a thermostat at 50 ºC 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. 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-dinitrophenyl hydrazone derivative is 253 ºC (lit. m.p. 248 ºC).

RESULTS AND DISCUSSION

The kinetics of oxidation of benzyl ethers by 1-chlorobenzotriazole is investigated at several initial concentrations of the reactants. Under the condition [CBT] << [benzyl ether], the oxidation of benzyl ether by 1-chlorobenzotriazole proceeds smoothly at 50 ºC in aqueous acetic acid. The plot of log [CBT] against time is found to be linear showing a first order dependence on [CBT]. The constancy of pseudo first-order rate constant at different [substrate] at constant [CBT] indicates that the reaction is zero order in [substrate] (Table-1).

TABLE-1
EFFECT OF VARYING [BENZYL ETHERS] ON THE REACTION RATE AT 323 K
$[CBT] = 2.0 \times 10^{-3}$ M, $[HClO_4] = 0.5$ M; Solvent (v/v) = 70 % CH_3COOH-30 % H_2O

[Benzyl ether] $\times 10^2$ M	$k_{obs} \times 10^4$ s^{-1}				
	Benzyl *n*-propyl ether	Benzyl *iso*-propyl ether	Benzyl *n*-butyl ether	Benzyl *iso*-butyl ether	Benzyl *t*-butyl ether
1.0	5.93	5.94	5.84	5.81	5.80
2.0	6.02	6.04	6.12	6.21	6.06
2.5	6.25	6.23	6.19	6.27	6.24
3.0	6.14	6.18	6.08	6.05	6.09

The effect of $[H^+]$ is investigated by varying $[HClO_4]$. Increase of $[H^+]$ ion increases the rate constant of the reaction (Table-2). The plot of log k_{obs} *versus* log $[H^+]$ is linear with unit slope (r = 0.99) indicating first order dependence on $[HClO_4]$.

TABLE-2
EFFECT OF VARYING $[HClO_4]$ ON THE REACTION RATE AT 323 K
[Benzyl ether] $= 2.0 \times 10^{-2}$ M, $[CBT] = 2.0 \times 10^{-3}$ M; Solvent (v/v) = 70 %
CH_3COOH-30 % H_2O

$[HClO_4]$ M	$k_{obs} \times 10^4$ s^{-1}				
	Benzyl *n*-propyl ether	Benzyl *iso*-propyl ether	Benzyl *n*-butyl ether	Benzyl *iso*-butyl ether	Benzyl *t*-butyl ether
0.1	1.20	1.20	1.22	1.24	1.21
0.2	2.41	2.42	2.44	2.48	2.42
0.4	4.80	4.84	4.88	4.96	4.84
0.5	6.02	6.04	6.12	6.21	6.06

The increase in percentage of acetic acid in the reaction mixture decreases the rate (Table-3). Plot of log k_{obs} *versus* 1/D (D is the dielectric constant of the medium) is found to be linear (r = 0.94).

TABLE-3
EFFECT OF VARYING SOLVENT COMPOSITION ON
THE REACTION RATE AT 323 K
[Benzyl ether] $= 2.0 \times 10^{-2}$ M, $[CBT] = 2.0 \times 10^{-3}$ M $[HClO_4] = 0.5$ M

CH_3COOH-H_2O % (v/v)	D	$k_{obs} \times 10^4$ s^{-1}				
		Benzyl *n*-propyl ether	Benzyl *iso*-propyl ether	Benzyl *n*-butyl ether	Benzyl *iso*-butyl ether	Benzyl *t*-butyl ether
50-50	37.50	8.05	8.08	8.12	8.01	8.12
60-40	31.50	7.04	7.08	7.13	7.14	7.10
70-30	27.00	6.02	6.04	6.12	6.21	6.06
80-20	20.00	5.05	5.16	5.10	5.05	5.18

Effect of added benzotriazole on the rate of the reaction is studied at different initial concentrations of benzotriazole. Addition of benzotriazole has no effect on the rate of oxidation. The reaction mixture fails to initiate polymerization of methyl methacrylate solution, indicating the absence of free radicals.

The oxidation of benzyl ethers is studied at different temperatures (Table-4). Arrhenius plot of log k_{obs} *vs.* 1/T is linear (r = 0.99). The energy of activation (Ea), enthalpy of activation ($\Delta H^{\#}$), free energy of activation ($\Delta G^{\#}$), entropy of activation ($\Delta S^{\#}$) and pre-exponential factor A are calculated (Table-5).

TABLE-4
EFFECT OF TEMPERATURE ON THE REACTION RATE
[Benzyl ether] = 2.0×10^{-2} M, [CBT] = 2.0×10^{-3} M, [HClO$_4$] = 0.5 M,
Solvent (v/v) = 70 % CH$_3$COOH – 30 % H$_2$O

Temp. (K)	$k_{obs} \times 10^4$ s^{-1}				
	Benzyl *n*-propyl ether	Benzyl *iso*-propyl ether	Benzyl *n*-butyl ether	Benzyl *iso*-butyl ether	Benzyl *t*-butyl ether
308	1.64	1.55	1.62	1.57	1.60
313	2.91	2.96	3.04	2.94	2.98
318	4.56	4.57	4.43	4.49	4.59
323	6.02	6.04	6.12	6.21	6.06

TABLE-5
ACTIVATION PARAMETERS FOR THE OXIDATION OF BENZYL ETHERS AT 323 K

Benzyl ethers	Ea (kJ mol^{-1})	A (s^{-1})	$\Delta H^{\#}$ (kJ mol^{-1})	$\Delta G^{\#}$ (kJ mol^{-1})	$\Delta S^{\#}$ (JK^{-1} mol^{-1})
Benzyl *n*-propyl ether	68.15	6.29×10^7	65.46	136.97	-221.40
Benzyl *iso*-propyl ether	68.97	8.57×10^7	66.28	138.16	-222.53
Benzyl *n*-butyl ether	69.34	9.96×10^7	66.65	138.67	-222.98
Benzyl *iso*-butyl ether	69.12	9.31×10^7	66.43	138.34	-222.63
Benzyl *t*-butyl ether	68.97	8.59×10^7	66.28	138.15	-222.52

Mechanism: The most possible mechanism for the oxidation of benzyl ethers by 1-chlorobenzotriazole involves the protonation of 1-chlorobenzotriazole in the rate determining step followed by the interaction with ether to give the products. A similar mechanism has been proposed for the oxidation of benzaldehyde by 1-chloro-benzotriazole[9] and oxidation of alcohols by NCS[18].

The rate of the reaction decreases with increasing acetic acid content in the solvent medium *i.e.*, with decreasing dielectric constant of the reaction medium. This is indicative of the interaction between a positive ion and a neutral molecule[5]. The increase of rate with the increase in the dielectric constant of the medium is due to the formation of charged species[19]. The constancy of free energy of activation values supports the operation of unified mechanism in all the benzyl ethers.

As the rate increases with increase in [HClO$_4$], it is presumed that CBTH$^+$ acts as the effective oxidizing species in the present investigation. Initially 1-chloro-benzotriazole gets protonated in the slow step to give CBTH$^+$ which then reacts with the substrate in the fast step to give the product.

$$CBT + H^+ \xrightarrow[\text{slow}]{\textbf{k}_1} CBTH^+$$

$$C_6H_5CH_2OR + CBTH^+ \xrightarrow{\text{fast}} C_6H_5CHO + BT + RCl$$
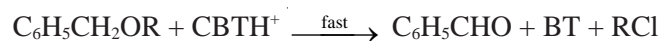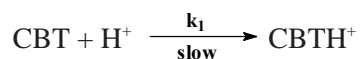
R = alkyl groups.

The rate law takes the form:

$$-d[CBT]/dt = k_1[CBT][H^+]$$

The rate law predicts the first order dependence on [CBT], [H⁺] and the zero-order dependence on [benzyl ether].

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