

Oxidative bromination of acetophenones by Oxone in presence of bromide ion : Kinetic and mechanistic study

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Abstract

The oxidative bromination of acetophenones by Oxone in presence of bromide ion was carried out in 50% aqueous acetic acid solution under pseudo-first-order conditions keeping large excess of acetophenone over that of oxidant. The reaction between Oxone and bromide generating bromine occurs in a prior equilibrium which is the reactive species. The bromine thus generated acts as a brominating reagent and forms an intermediate complex with acetophenone. The electrophilic attack of Br₂ on carbon atom is the rate-determining step. The rapid decomposition of intermediate takes place to give α -bromoacetophenone as the product. Based on the observed results plausible mechanism is proposed and the related rate law has been deduced.

Keywords: Acetophenones, Bromination, Oxone, Bromide, Kinetics

Introduction

Bromination of organic substrates, particularly aromatics, has gained a significant amount of attention in recent years owing to the commercial importance of such compounds as potent antitumor, antibacterial, antifungal, antineoplastic, antiviral and antioxidizing agents and also as industrial intermediates for the manufacture of speciality chemicals, pharmaceuticals and agrochemicals[1]. Unfortunately, the hazards associated with traditional bromination are not trivial and cannot be ignored. Environmental problems caused by the use of detrimental chemicals and solvents in classical bromination methods and the anticipated legislations against their use are some of the major concerns. Consequently, what is needed is a methodology that would be environmentally friendly and clean and yet efficient, site selective, operationally simple and cost-effective. The bromoderivatives of carbonyl compounds, especially α -bromo ketones are utilized in synthesis of variety of biologically important molecules. Bromoorganics also constitute various industrial products such as pesticides, herbicides

and fire retardants[2]. The general methods of bromination of organic compounds such as use of either molecular bromine or its complex with organic ammonium salts. The hazardous nature of elemental bromine and difficulties encountered in its handling has led to preparation[3] of new active bromine reagents like tetraalkylammonium tribromides. These reagents can be synthesized[4] very easily by oxidizing bromide to tribromide and then precipitating with quaternary ammonium cation. The tetraalkylammonium polyhalides have been used in various organic transformations[5-14]. Apart from the above uses of quaternary ammonium polyhalides these reagents have also been used for oxidation of various organic and inorganic substrates[15,16]. The general mechanism of the reactions involves a complex formation between the substrate and tribromide ion followed by its decomposition. The decomposition of complex formed may proceed either by direct two electron transfer between the reactants or by hydride ion transfer. The combination of an oxidant like hydrogen peroxide[17], sodium periodate[18] and

Oxone[19] in presence of bromide can also be used for the oxidative brominations of ketone. But there seems to be no study on the mechanism of such oxidative brominations, although, the methods developed have been claimed to be green as compared with that involving bromine and tetraalkyl ammonium salts. In continuation of our work[20-22] on use of bromine reagents, the present study on oxidative bromination of acetophenones by Oxone and potassium bromide and understanding of the mechanism was undertaken.

Experimental:

Materials and methods

All the chemicals used were of reagent grade and doubly distilled water was used throughout. The solutions of acetophenone(SD fine) were prepared by dissolving them in 50 % V/V acetic acid–water mixtures. The acetic acid (Thomas Baker) was distilled with usual method[23] and used. Potassium bromide (SD fine) was used throughout the study as received.

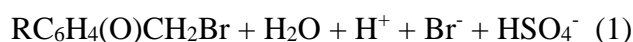
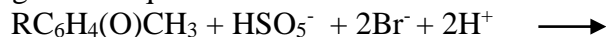
Kinetic studies

Kinetic runs were carried out under pseudo-first-order conditions keeping large excess of acetophenone. The solutions containing the reactants and all other constituents were thermally equilibrated at $25 \pm 0.1^\circ\text{C}$ separately, mixed and the reaction mixture was analyzed for unreacted Oxone by iodometrically. The values of rate constants are reproducible within $\pm 5\%$.

Product analysis and stoichiometry

The product analysis was carried out by using the acetophenone (4 m mol) and Oxone (1.0 mmol). Reactants were taken in acetic acid-water (1:1, V/V) and the reaction mixture was allowed to stand for 24 hours to ensure completion of the reaction. Then the reaction mixture was extracted with ether and the acetic acid in the ether layer was neutralized by using saturated sodium bicarbonate solution (NaHCO_3)

and washed with distilled water. Then ether layer was separated and evaporated to obtain α -bromoacetophenone as the product. The product α -bromoacetophenone was confirmed by boiling point. (b p 134°C , lit.b.p = 135°C). Similarly the product analysis for the oxidation products of p-substituted acetophenones was carried out. The products were the corresponding α -bromoacetophenone. The observed physical constants (M.P. / B.P.) of the corresponding products are given in (Table 1). Therefore, the stoichiometry of the present reaction would be as given in equation 1.



Results

Effect of reactants

The effect of oxidant, Oxone, and substrate, acetophenones, were studied at 25°C by keeping all other conditions constant. The [acetophenone] and [oxidant] were varied from 1.0×10^{-2} to $1.0 \times 10^{-1} \text{ mol dm}^{-3}$ and 2.0×10^{-4} to $2.0 \times 10^{-3} \text{ mol dm}^{-3}$ at constant [oxidant] of $2.0 \times 10^{-3} \text{ mol dm}^{-3}$ and [Acetophenone] of $2.0 \times 10^{-2} \text{ mol dm}^{-3}$ respectively. A constant concentration of KBr was maintained at $2.0 \times 10^{-3} \text{ mol dm}^{-3}$ while studying the effect of oxidant and substrate. The pseudo-first-order plots of $\log[\text{Oxidant}]$ against time were linear and the values of pseudo-first-order rate constants, k_{obs} , remain constant (Table 2) when the concentration of oxidant is varied indicating first order dependence of the reaction on the oxidant concentration. While the values of pseudo-first-order rate constants, k_{obs} , were found to be increased as concentration of substrate increases. (Table 3) and the plot k_{obs} against [Substrate] were also found to be linear without any intercept indicating the first order

dependence of the reaction on the substrate concentration.

Table - 1 Product analysis and characterization for oxidative bromination of acetophenones by Oxone in presence of bromide ion.

	Reactant	Product	B. P/ M.P (°c)	Lit. B. P/ M.P(°c)
1	Acetphenone	α -bromo acetophen one	134	135
2	p-methyl acetophenone	p-methyl α -bromo acetophen one	105	105
3	p-chloro acetophenone	p-chloro α -bromo acetophen one	94	93-96
4	p-hydroxy acetophenone	p-hydroxy α -bromo acetophen one	125	123-126
5	p-methoxy acetophenone	p-methoxy α -bromo acetophen one	70	69-71

Effect of concentration of KBr

The concentration of KBr, was varied between $0.4 \times 10^{-3} \text{ mol dm}^{-3}$ to $4.0 \times 10^{-3} \text{ mol dm}^{-3}$

keeping all other concentrations constant. The pseudo-first-order rate constants, k_{obs} , increases (Table 4) with increase in concentration of KBr for all the substrates. The plot of k_{obs} against [KBr] were also found to be linear without any intercept indicating that reaction did not occur in absence of KBr under the reaction conditions and also first order dependence of the reaction on the KBr concentration.

Effect of hydrogen ion concentration

The hydrogen ion concentration was studied by varying sulphuric acid between $0.7 \times 10^{-2} \text{ mol dm}^{-3}$ to $7.0 \times 10^{-2} \text{ mol dm}^{-3}$ keeping all other concentrations constant. There was no change in the values of k_{obs} as the sulphuric acid hydrogen ion concentration increases indicating that the reaction is independent of hydrogen ion concentration.

Effect of ionic strength and solvent composition (dielectric constant)

The effect of ionic strength and dielectric constant were studied by varying the concentration of KNO_3 and acetic acid respectively. The increase in ionic strength between 3.6×10^{-2} to $1.06 \times 10^{-1} \text{ mol dm}^{-3}$ did not affect the k_{obs} values. The variation of dielectric constant on the rate of the reaction was studied by varying the % of acetic acid was from 50 to 90. The values of k_{obs} of both the alcohols decreases as the % acetic acid increases.

Effect of temperature

The activation parameters for the reactions were determined by studying the reaction at 293, 298, 303, 308 and 313 K. The activation energy and activation enthalpy were calculated from the plots of $\log k_{\text{obs}}$ and $\log (k_{\text{obs}}/ T)$ against $(1/T)$ plots and given in Table 5.

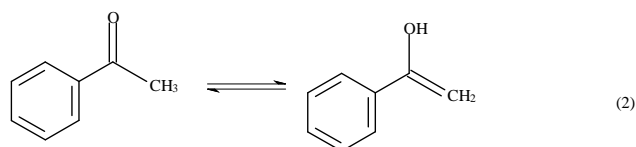
Discussion

Mechanism and rate law

The reaction was carried out under pseudo-first-order conditions keeping the large

excess concentration of acetophenones in 50% acetic acid solutions. The pseudo-first-order plot was found to be linear for all the kinetic runs studied and rate constants, k_{obs} , value remained constant when the concentration of the oxidant, Oxone, was varied from 0.2×10^{-3} to 2.0×10^{-3} mol dm^{-3} at constant concentration of acetophenone of 0.02 mol dm^{-3} indicating first order dependence of the reaction on the oxidant concentration; while the pseudo-first-order rate constant was found to be increased with increase in the concentration of acetophenone between concentration range of 1.0×10^{-2} to 1.0×10^{-1} mol dm^{-3} at the constant concentration of bromide at 2.0×10^{-3} mol dm^{-3} . The order in reductant concentration was found to be unity as the plots of k_{obs} against [acetophenone] are found to be linear without any intercept.

In acidic solutions the acetophenone undergoes fast enolization[23] as represented by equation (2). The reaction between the Oxone and the bromide ion generates bromine in the acidic medium as explained in the earlier chapters. The formation of bromine was also examined by UV-VIS spectrophotometry



in 50 % V/V acetic acid with an absorption peak at 394 nm at which only bromine will absorb. Therefore, the initiation of the bromination of acetophenones occurs by the generation of bromine in prior equilibria which then react with the substrates as shown in the below Scheme 1. The interaction between the bromine and the enol form of the acetophenone occurs through

electrophilic attack of Br_2 , on the nucleophilic α -carbon atom of the carbonyl group. The intermediate thus formed undergoes decomposition to give the corresponding α -bromoacetophenone. The detailed mechanism of the reaction can be represented as in Scheme 1. The corresponding rate law according to the Scheme 1 will be given by equation (3). Substituting for the $[Br_2]$ form first and second equilibrium of Scheme 1 we get equation (4). The corresponding expression for k_{obs} is given by equation (5).

$$\text{Rate} = k_1 [\text{Acetophenone}][Br_2] \quad (3)$$

$$\text{Rate} = k_1 K_1 [\text{Acetophenone}][HSO_5^-][Br^-] \quad (4)$$

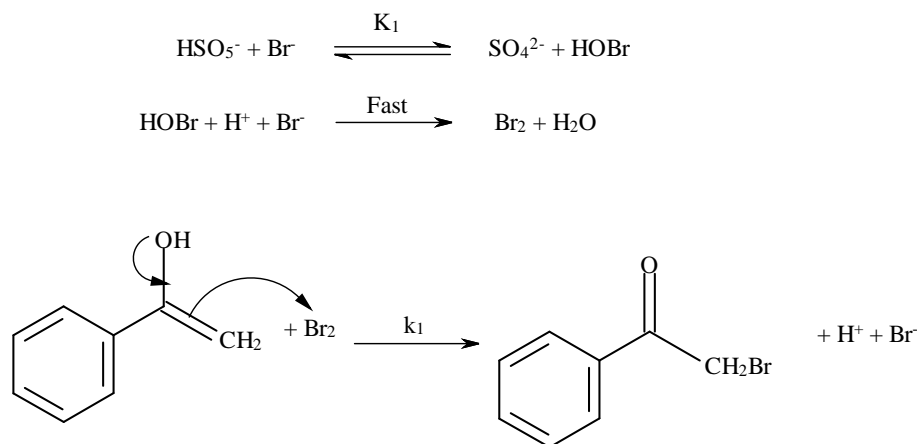
$$k_{obs} = \text{Rate} / [HSO_5^-] \\ = k_1 K_1 [\text{Acetophenone}] [Br^-] \quad (5)$$

The expression (5) can be verified by plotting k_{obs} against [Acetophenone] and $[Br^-]$ which were found to be linear thus supporting the mechanism proposed.

The ΔG^\ddagger values for all the acetophenones studied are around 95 kJ mol^{-1} for all para substituted acetophenones indicate the similarity in the mechanism. The fairly high positive value of ΔH^\ddagger indicates that, the transition state is highly solvated, while the high negative value of entropy favours the formation of a compact and a more ordered transition state. There was also no effect of added acrylonitrile, a free radical scavenger, on reaction suggesting a mechanism without any free radical intervention. The increase in the acetic acid content was found to decrease the rate of reaction. Since the reactant does not undergo protonation, the effect of acetic acid is due to the decrease in solvent polarity. The rate of the reaction decreases with increase in the acetic acid content; this is due to the decrease in the water content in the reaction mixture, which is essential for rate determining decomposition of the intermediate.

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Scheme 1. Mechanism of oxidative bromination of acetophenones by Oxone in presence of bromide.

Table – 2. Effect of concentration of Oxone on the k_{obs} values of oxidative bromination of acetophenones by in presence of bromide ion at 25°C.

$10[\text{Acetophenone}] = 2.0 \text{ mol dm}^{-3}$, $10^3[\text{KBr}] = 2.0 \text{ mol dm}^{-3}$, $10^2[\text{H}_2\text{SO}_4] = 3.0 \text{ mol dm}^{-3}$,
 $I = 0.1 \text{ mol dm}^{-3}$

$10^3[\text{Oxone}]$ mol dm ⁻³	$10^4 k_{\text{obs}} \text{ s}^{-1}$				
	Acetophenone	p-methyl acetophenone	p-chloro acetophenone	p-hydroxy acetophenone	p-methoxy acetophenone
0.2	1.07	1.34	1.27	4.77	6.76
0.4	1.07	1.34	1.27	4.76	6.75
0.6	1.10	1.34	1.28	4.75	6.72
0.8	1.09	1.32	1.26	4.75	6.77
1.0	1.08	1.33	1.27	4.76	6.75
2.0	1.09	1.34	1.29	4.78	6.76

Table – 3. Effect of concentration of acetophenones on the k_{obs} values of their oxidative bromination by Oxone in presence of bromide ion at 25°C.

$10^3[\text{Oxone}] = 2.0 \text{ mol dm}^{-3}$, $10^3[\text{KBr}] = 2.0 \text{ mol dm}^{-3}$, $10^2[\text{H}_2\text{SO}_4] = 3.0 \text{ mol dm}^{-3}$,
 $I = 0.1 \text{ mol dm}^{-3}$

[Acetophenone] mol dm ⁻³	$10^4 k_{\text{obs}} \text{ s}^{-1}$				
	Acetophenone	p-methyl acetophenone	p-chloro acetophenone	p-hydroxy acetophenone	p-methoxy acetophenone
0.01	0.34	0.56	0.59	1.80	2.30
0.02	1.07	1.34	1.27	4.76	6.75
0.04	1.94	2.34	2.08	7.56	9.67
0.06	2.76	3.41	3.19	10.4	15.5
0.08	3.54	4.72	4.31	14.3	20.7
1.0	5.12	6.34	5.72	18.1	26.5

Table – 4. Effect of concentration of KBr on the k_{obs} values of oxidative bromination of acetophenones by Oxone in presence of bromide ion at 25°C.

$10^3[\text{Oxone}] = 2.0 \text{ mol dm}^{-3}$, $10[\text{Acetophenone}] = 2.0 \text{ mol dm}^{-3}$, $10^2[\text{H}_2\text{SO}_4] = 3.0 \text{ mol dm}^{-3}$, $I = 0.1 \text{ mol dm}^{-3}$

$10^3[\text{KBr}]$ mol dm^{-3}	$10^4 k_{\text{obs}} \text{ s}^{-1}$				
	Acetophenone	p-methyl acetophenone	p-chloro acetophenone	p-hydroxy acetophenone	p-methoxy acetophenone
0.4	0.18	0.32	0.34	0.77	1.11
0.6	0.31	0.44	0.42	1.27	1.65
0.8	0.45	0.67	0.54	1.73	2.45
1.0	0.62	0.86	0.69	2.30	3.45
1.5	0.86	1.17	0.92	3.68	5.41
2.0	1.07	1.34	1.27	4.76	6.75
2.5	1.38	1.78	1.61	6.34	9.40
3.0	1.68	2.35	1.99	7.55	10.9
3.5	2.05	2.65	2.34	9.10	12.7
4.0	2.35	3.01	2.61	10.4	14.6

Table – 5. Activation parameters for oxidative bromination of acetophenones by Oxone in presence of bromide ion in 50 % V/ V/ acetic acid.

$10^3[\text{Oxone}] = 2.0 \text{ mol dm}^{-3}$, $10[\text{Acetophenone}] = 2.0 \text{ mol dm}^{-3}$, $10^3[\text{KBr}] = 2.0 \text{ mol dm}^{-3}$, $10^2[\text{H}_2\text{SO}_4] = 3.0 \text{ mol dm}^{-3}$, $I = 0.1 \text{ mol dm}^{-3}$.

	Acetophenone	p-methyl acetophenone	p-chloro acetophenone	p-hydroxy acetophenone	p-methoxy acetophenone
Ea kJ mol ⁻¹	51.5	54.1	52.4	55.2	52.4
ΔH^\ddagger kJ mol ⁻¹	49.4	51.7	49.9	53.4	49.9
ΔG^\ddagger kJ mol ⁻¹	100.3	99	83.9	96.3	95.1
$-\Delta S^\ddagger$ J mol ⁻¹ K ⁻¹	171	159	167	144	95