



Asian Journal of Research in Chemistry and Pharmaceutical Sciences

Journal home page: www.ajrcps.com



KINETIC STUDY OF OXIDATION OF 4-HYDROXY ACETOPHENONE BY TETRABUTYL AMMONIUM TRIBROMIDE IN ACIDIC MEDIA

Ravindra Shimpi^{*1}

^{1*}Badrinarayan Barwale Mahavidyalaya, Jalna, Maharashtra, India.

ABSTRACT

Oxidation of 4-hydroxy acetophenone by tetrabutylammoniumtribromide in 1:1 aqueous acetic acid medium has been investigated at 27°C spectrophotometrically. Stoichiometric result showed that one mole of tetrabutylammoniumtribromide was consumed for one mole of 4-hydroxyacetophenone. Kinetic study indicated that reaction shows first order dependence on concentration of oxidant and first order dependence on concentration of 4-hydroxyacetophenone. Increase in acid concentration decreases the rate of reaction. The activation parameters of the oxidation process have been investigated by studying reaction from 283 to 323K. Mechanism involving formation of complex between oxidant and 4-hydroxyacetophenone has been proposed. Final product was analyzed and identified from its melting point, chromatography and spectroscopically as 2-bromo-4'-hydroxy acetophenone. Based on the kinetic data and product analysis probable mechanism was proposed.

KEYWORDS

Kinetics, Oxidation, 4-hydroxy acetophenone (4-HAP), Oxidant and Tetrabutylammoniumtribromide (TBATB).

Author for Correspondence:

Ravindra Shimpi,
Badrinarayan Barwale Mahavidyalaya,
Jalna, Maharashtra, India.

Email: raviindra336@gmail.com

INTRODUCTION

Tetraalkylammonium polyhalides are comprehensively used as halogenating and oxidizing reagents in synthetic organic chemistry¹⁻⁶. Cetylpyridinium tribromide an environmentally benign reagent also used for organic brominations and acetylations⁷. An efficient microwave induced solvent free organic bromination using TBATB was also carried⁸. These compounds are more suitable than molecular halogens due to their solid state, easy handling, stable nature, selectiveness and higher yield of products. In recent times, tetrabutylammonium tribromide (TBATB) has been

used for the bromination of number of organic compound. Bromination of organic substrates mainly aromatic substrates has gained a significant interest in recent years because of marketable significance of these compounds as an effective antitumor, antibacterial, antifungal, antineoplastic, antiviral, antioxidizing agents and also as industrial intermediate for the manufacture of essential chemicals, pharmaceuticals and agrochemicals⁹. Bromo derivatives of carbonyl compounds, mainly α -bromo ketones are used in synthesis of various biologically significant compounds. Important compounds like pesticides, herbicides and fire retardants¹⁰ used in industries. Less hazardous effect of organic ammonium bromide and to prepare environment friendly bromo derivatives make their use as a selective brominating reagent compared to molecular bromine. Owing to hazardous nature of bromine, difficulty in handling has led to develop new active brominating agent like tetraalkylammonium tribromide¹¹, which can be prepared by oxidizing bromide to tribromide and then precipitating with quaternary ammonium cation. Literature reveals bromination of various organic compounds such as α -amino acid¹² using tetraalkylammonium polyhalides like TBATB, Aryl thiourea to 2-aminobezothiazole¹³, carbonyl compounds to 1, 3-oxothioalanes¹⁴, synthesis of aurones¹⁵, tetrahydropyranylation or depyranylation¹⁶, thioacetalisations and trans-thioacetalisations¹⁷, cleavage of dithioacetals¹⁸, preparations of thiosugars¹⁹, transformation of tolyl sulfones to quinodimethanes²⁰, germinal diacylations²¹, cleavage of tert-butyl dimethylsilylethers²², oxidation of aliphatic aldehydes²³, α -hydroxy acids²⁴, oxidative generation of carbonyl compounds from oximes²⁵, oxidation of formic and oxalic acid²⁶, oxidations of various organic and inorganic substrates²⁷⁻³¹ by TBATB.

The main reactive species is Br_3^- formed from dissociation of TBATB further dissociates to bromide ion and molecular bromine which can be suppressed by adding excess bromide ion. Additional bromide ion affects the rate of reaction in almost all cases except in phosphorous acids²⁸.

Mechanism involves formation of complex between the tribromide ion and substrate followed by its decomposition via direct two electron transfer between reactants or by hydride ion transfer. The path involving single electron transfer was discarded due to negative effect of free radical test. Various other oxidants also oxidize acetophenones to α -bromo acetophenones has already been accounted in literature¹¹. Literature shows oxidative bromination of acetophenones by oxone in presence of bromide ion was also carried out in 50% aqueous acetic acid solution³². In continuation of earlier work³³ on this substrate the present study was undertaken to evaluate the oxidative and brominating power of the said oxidant on 4-hydroxy acetophenone.

EXPERIMENTAL

MATERIAL

TBATB was prepared by reported synthesis method and its purity was checked by both iodometric and spectrophotometric method. Commercial product 4-hydroxy acetophenone (sd Fine) of highest purity was used as supplied. Acetic acid (Merck) was used for the study. Pure potassium bromide (sd Fine) was used during entire study.

Kinetic Runs

In all kinetic runs for preventing dissociation of tribromide ion a fixed amount (0.015 mol dm^3) of KBr is added in reaction mixture. Pseudo first order conditions maintained by taking large excess of 4-hydroxy acetophenone over oxidant TBATB. All the constituents of the reactions were thermally equilibrated at $27 \pm 0.5^\circ\text{C}$ using 'Toshniwal' make thermostat. The reaction mixture was analyzed for TBATB at 394 nm using Elico BL-198 UV-Visible double beam Biospectrophotometer. The values of rate constants are reproducible within $\pm 4\%$ (Table No.1) and corresponding pseudo first order graphs are also plotted.

Product analysis and stoichiometry

For product analysis reaction was carried out by taking 4-hydroxy acetophenone (3 m mole) and TBATB (1 m mole) in acetic acid-water (1:1 V/V) and the reaction mixture was allowed to stand for 1 day to completion. Reaction mixture was then

extracted with ether and excess acetic acid in ether layer was neutralized by saturated solution of sodium bicarbonate (NaHCO_3) and washed using distilled water. Then ether layer was then separated and evaporated to obtain the final product. The final product was identified as 2-bromo-4'-hydroxy acetophenone and confirmed by its melting point as 126°C , chromatography and spectroscopically. To determine stoichiometry TBATB (2 m mole) and 4-hydroxy acetophenone (1 m mole) were mixed in 1:1 (V/V) acetic acid water, this reaction mixture was allowed to stand for a day and the unreacted TBATB was determined spectrophotometrically at 394nm. The reaction stoichiometry was found to be 1:1.

Effect of variation of reactants

The effect of variation of oxidant and substrate were studied at 27°C maintaining other conditions constant. The [TBATB] was varied from 1×10^{-3} to 10×10^{-3} mole/ dm^3 and [4-hydroxyacetophenone] was varied from 1×10^{-2} to 10×10^{-2} mole/ dm^3 . The rate constant remains constant with increase in [oxidant] indicating first order dependence on oxidant. The rate constant increases with increase in [substrate] indicating first order dependence on substrate (Table No.1), (Figure No.1 and 2).

Effect of variation of [Acetic acid]

The effect of variation in [Acetic acid] was carried by varying acid content in reaction mixture between 10 to 50 % V/V. The pseudo first order rate constant decreases with increase in [acid] (Table No.1), (Figure No.3).

Effect of free radical scavenger

In order to investigate the involvement of free radicals^{34,35} the reaction was studied in presence of free scavenger acrylonitrile, no polymerization takes place in reaction mixture suggesting absence of free radical formation during reaction (Table No.1) (Figure No.4).

Effect of variation of temperature

Effect of temperature on reaction mixture was studied by varying temperature between 10, 20, 30, 40 and 50°C respectively. The rate constant was found out and thermodynamic parameters E_a , ΔH^\ddagger , ΔG^\ddagger and ΔS^\ddagger were determined (Table No.2) (Figure No.5).

DISCUSSION

The reaction was carried out under pseudo first order conditions keeping large excess of substrate 4-hydroxyacetophenone over oxidant TBATB in 1:1 aqueous acetic acid solution and having 0.015 mole/ dm^3 of KBr to prevent dissociation of tribromide into bromide ion and bromine molecule. Pseudo first order rate constant k_{obs} increased linearly during variation of [oxidant] from 1×10^{-3} to 10×10^{-3} mole/ dm^3 at constant [4-hydroxyacetophenone] = 3×10^{-2} mole/ dm^3 suggesting first order dependence of reaction on [oxidant] (Figure No.2). While k_{obs} increased with increase in [4-hydroxy acetophenone] which is varied from 1×10^{-2} to 10×10^{-2} mole/ dm^3 at constant [TBATB] = 1×10^{-3} mole/ dm^3 . Plot of \log [4-hydroxyacetophenone] versus $\log k_{\text{obs}}$ was obtained linear with slope 1.02 suggesting first order dependence of reaction on substrate concentration (Figure No.1).

4-hydroxyacetophenone undergoes rapid enolisation^{36,37} as below,

Oxidant TBATB attacks the enol form of the substrate through electrophilic attack on Br_3^- on α -carbon atom of carbonyl group. The intermediate complex formed undergoes decomposition to give the final product as 2-bromo-4'-hydroxyacetophenone as represented in mechanism. The presence of hydroxy group at 4' position (para) acting as e^- withdrawing increases the rate of reaction due to development of positive charge on intermediate complex as in mechanism. The reasonable value of ΔG^\ddagger and the linearity of plot between $-\log k_{\text{obs}}$ versus $1/T$ (Figure No.5) additionally support the mechanism. A free radical scavenger-acrylonitrile when added to the reaction mixture shows absence of precipitation and polymerization suggesting involvement of two electron complementary step in mechanism. Increase in acid concentration decreases reaction rate indicating absence of protonation of 4-hydroxyacetophenone which in turn supports the decreased solvent polarity. With decreased solvent polarity along with decreased water content further supports decomposition of intermediate complex in slow and rate determining step.

The rate law for the reaction can be expressed as in equation (1)

$$\text{Rate} = k [\text{TBATB}] [\text{4-hydroxyacetophenone}] \dots(1)$$

In terms of pseudo first order rate constant rate law can be expressed as in equation (2)

$$\text{Rate}/[\text{TBATB}] = k_{\text{obs}} = k [\text{4-hydroxyacetophenone}] \dots(2)$$

Activation parameters like energy of activation E_a , enthalpy of activation ΔH^\ddagger , Gibb's free energy ΔG^\ddagger and entropy ΔS^\ddagger can be calculated from the slopes of plot $-\log k_{\text{obs}}$ versus $1/T$ (Arrhenius plots) (Figure No.5). Considerable value of entropy supports the formation of ionic intermediate complex between oxidant and substrate.

High negative value of entropy of activation ΔS^\ddagger further supports more compact and ordered transition state formation. High positive value of enthalpy of activation ΔH^\ddagger suggests formation of highly solvated transition state (Table No.5).

Table No.1: Effect of variation of reactants on reaction between 4-HAP and TBATB in 1:1 acetic acid at 27°C

[KBr] = 1.5x10⁻² mole/dm³

[4-HAP]1x10 ⁻² mole/dm ³	[TBATB]1x10 ⁻³ mole/dm ³	[Acetic acid] % (V/V)	[Acrylonitrile] % (V/V)	k _{obs} 1x10 ⁻³ (s ⁻¹)
1	1	25	0	0.45
3	1	25	0	0.51
5	1	25	0	0.57
7	1	25	0	0.60
9	1	25	0	0.66
10	1	25	0	0.72
3	1	25	0	0.70
3	3	25	0	0.69
3	5	25	0	0.71
3	7	25	0	0.70
3	9	25	0	0.69
3	10	25	0	0.70
3	1	10	0	0.68
3	1	20	0	0.60
3	1	30	0	0.51
3	1	40	0	0.42
3	1	50	0	0.38
3	1	25	10	0.68
3	1	25	20	0.66
3	1	25	30	0.67
3	1	25	40	0.65
3	1	25	50	0.67
3	1	25	60	0.65

Table No.2: Effect of variation of temperature on reaction between 4-HAP and TBATB in 1:1 aqueous acetic acid at 27°C

[TBATB] = 1×10^{-3} mole/dm³ [4-HAP] = 3×10^{-2} mole/dm³ [KBr] = 1.5×10^{-2} mole/dm³
 $E_a^\# = -31.937$ KJ mole⁻¹

S.No	Temp.	T in Kelvin	K	$\Delta H^\#$ (KJ mole ⁻¹)	$\Delta S^\#$ (KJ mole ⁻¹)	$\Delta G^\#$ (KJ mole ⁻¹)
1	10°C	283	0.0035	-34.290	-0.1792	16.426
2	20°C	293	0.0047	-34.373	-0.1766	17.370
3	30°C	303	0.0060	-34.456	-0.1742	18.349
4	40°C	313	0.0100	-34.539	-0.1710	19.010
5	50°C	323	0.0200	-34.622	-0.1673	19.423
Average =			-34.456	-0.1736	18.115	

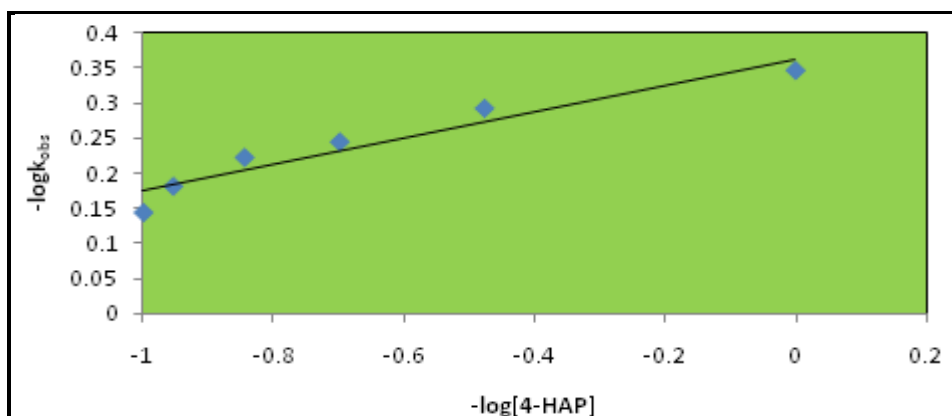
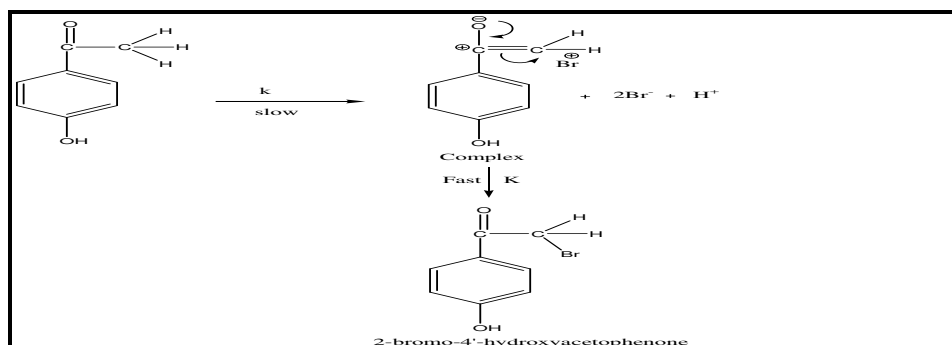
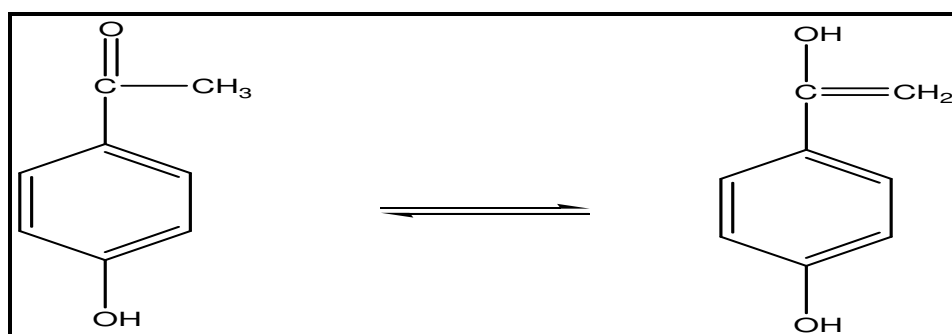


Figure No.1: Variation of $-\log k_{obs}$ versus $-\log[4-HAP]$

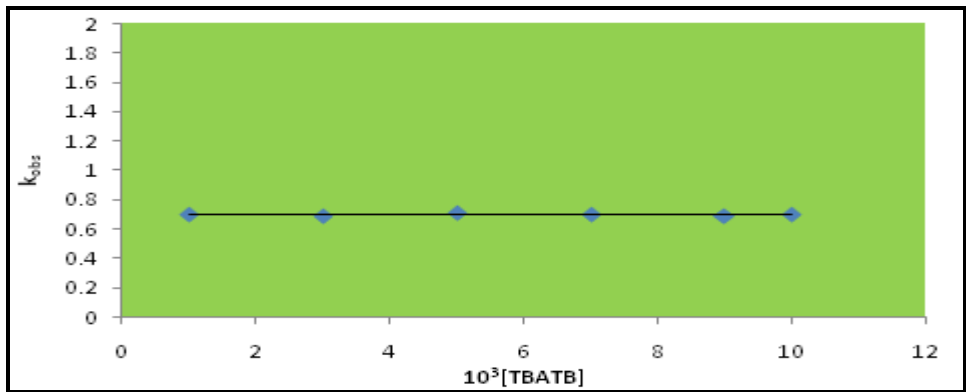


Figure No.2: Variation of k_{obs} versus [TBATB]

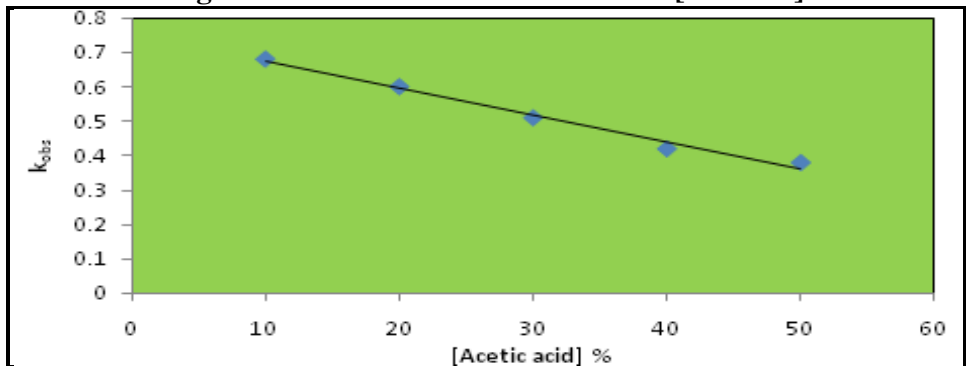


Figure No.3: Variation of k_{obs} versus [Acetic acid]

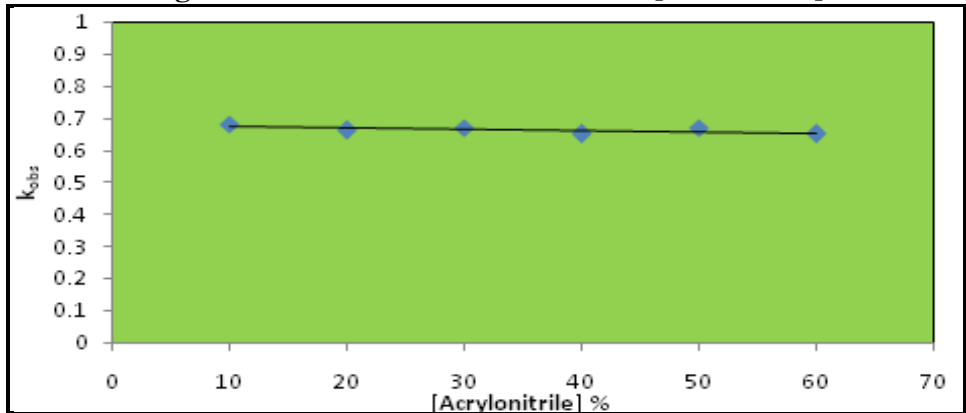


Figure No.4: Variation of k_{obs} versus [Acrylonitrile]

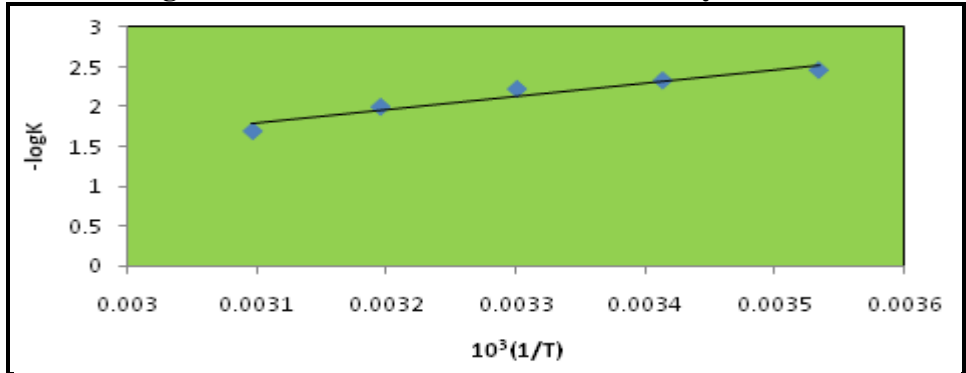


Figure No.5: Variation of $-\log k_{\text{obs}}$ versus $1/T$

CONCLUSION

Kinetic study of oxidation of 4-hydroxyacetophenone with TBATB was carried in 1:1 aqueous acetic acid under pseudo first order conditions keeping large excess of 4-hydroxyacetophenone over oxidant. The rate determining slow step involves an electrophilic attack of Br_3^- ion on carbonyl carbon of 4-hydroxyacetophenone to form the intermediate complex which rapidly decomposes to give final product as 2-bromo-4'-hydroxyacetophenone. Based on kinetic data and rate law suitable mechanism is proposed which is consistent with the observed results.

ACKNOWLEDGEMENT

The author is sincerely thanks to the Badrinarayan Barwale Mahavidyalaya, Jalna, Maharashtra, India for providing the facilities to complete this research work.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

BIBLIOGRAPHY

1. Kajigaeshi S, Kakinami T, Okamoto T and Fujisaki S. Synthesis of Bromoacetyl Derivatives by Use of Tetrabutylammonium Tribromide, *Bull. Chem. Soc. Japan*, 60(3), 1987, 1159-1160.
2. Kajigaeshi S, Kakinami T, Yamasaki H, Fujisaki S and Okamoto T. Halogenation Using Quaternary Ammonium Polyhalides. XI. Bromination of Acetanilides by Use of Tetraalkylammonium Polyhalides, *Bull. Chem. Soc. Japan*, 61(7), 1988, 2681-2683.
3. Buckles R E, Popov A I, Zelenszy W F and Smith R J. Spectrophotometric Study of Tetrabutylammonium Tribromide, *J. Am. Chem. Soc.*, 73(10), 1951, 4525-4528.
4. Bethalot J, Guette C, Ouchefoune M, Desbens P L and Besselier J J. A Convenient Synthesis of 3-Alkylthiophenes, *J. Chem. Res.(S)*, 1986, 381. *Synth. Commun*, 16(6), 1986, 689-696.
5. Kajigaeshi S, Kawamuki H and Fujisaki S. Oxidation Using Quaternary Ammonium Polyhalides. III. An Effective Oxidation of Alcohols and Ethers by the Use of Benzyltrimethylammonium Tribromide, *Bull. Chem. Soc. Japan*, 62(8), 1989, 2585-2588.
6. Kajigaeshi S, Morikawa Y, Fujisaki S, Kakinami T and Nishihira K. Oxidation Using Quaternary Ammonium Polyhalides. VIII. Oxidation of 1, 4-Benzenediols with Benzyltrimethylammonium Tribromide, *Bull. Chem. Soc. Japan*, 64(1), 1991, 336-338.
7. Anil kumar, Alimenla Jamir, Latonglila Jamir, Dipak Sinha and Upasana Bora Sinha. Cetylpyridinium tribromide-An environmentally benign reagent for organic brominations, *Org. Commun*, 4(1), 2011, 1-8.
8. Alimenla Bernard, Anil Kumar, Latonglila Jamir, Dipak Sinha and Upasana Bora Sinha. An Efficient Microwave-Induced Solvent-Free Organic Bromination Using Tetrabutylammonium Tribromide, *Acta. Chim. Slov*, 56(2), 2009, 457-461.
9. Kavala V, Naik S and Patel B K. A New Recyclable Ditribromide Reagent for Efficient Bromination under Solvent Free Condition, *J. Org. Chem*, 70(11), 2005, 4267-4271.
10. Bora M, Bose G, Chaudhari M K, Dhar S S, Gopinath R, Khan A T and B K Patel. Regioselective Bromination of Organic Substrates by Tetrabutylammonium Bromide Promoted by $\text{V}_2\text{O}_5\text{-H}_2\text{O}_2$: An Environmentally Favorable Synthetic Protocol, *Org. Lett*, 2(3), 2000, 247-249.
11. Rothenberg G, Beadnal R M H, McGrady G E and Clark J H. Competing bromination and oxidation pathways in acid bromate solutions: an experimental and theoretical study, *J. Chem. Soc., Perkin Trans*, 2(3), 2002, 630-635.
12. Raghvendra Shukla, Pradeep Sharma and Kalyan Banerji. Kinetics and mechanism of

- the oxidation of some neutral and acidic α -amino acids by tetrabutylammonium tribromide, *J. Chem. Sci.*, 116(2), 2004, 101-106.
13. Jordan A D, Luo C and Reitz A B. Efficient Conversion of Substituted Aryl Thioureas to 2-Aminobenzothiazoles Using Benzyltrimethylammonium Tribromide, *J. Org. Chem.*, 68(22), 2003, 8693-8696.
 14. Mondal E, Sahu P R, Bose G and Khan A T. A useful and convenient synthetic protocol for interconversion of carbonyl compounds to the corresponding 1,3-oxathiolanes and vice versa employing organic ammonium tribromide (OATB), *Tetrahedron Lett.*, 43(15), 2002, 2843-2846.
 15. Bose G, Mondal E and Khan A T, Bordoloi M. An environmentally benign synthesis of aurones and flavones from 2'-acetoxychalcones using n-tetrabutylammonium tribromide, *Tetrahedron Lett.*, 42(50), 2001, 8907-8909.
 16. Naik S, Gopinath R and Patel B K. Tetrabutylammonium tribromide (TBATB)-promoted tetrahydropyranylation/depyranylation of alcohols, *Tetrahedron Lett.*, 42(43), 2001, 7679-7681.
 17. Naik S, Gopinath R, Goswami M and Patel B K. Chemoselective thioacetalisation and transthoacetalisation of carbonyl compounds catalysed by tetrabutylammonium tribromide (TBATB), *Org. Biomol. Chem.*, 2(11), 2004, 1670-1677.
 18. Mondal E, Bose G and Khan A T. An expedient and efficient method for the cleavage of dithioacetals to the corresponding carbonyl compounds using organic ammonium tribromide (OATB), *Synth. Lett.*, 2001(6), 2001, 785-786.
 19. Wirching J and Voss J. Preparation of 2, 3, 5-Tri-O-benzyl-4-thio-L-arabino-furanosides and the Corresponding 4'-Thionucleoside Analogues, *Eur. J. Org. Chem.*, 1999(3), 1999, 691-696.
 20. Lenihan B D and Shechter H. Synthesis and Conversions of Substituted o-[(Trimethylsilyl)methyl]benzyl p-Tolyl Sulfones to o-Quinodimethanes and Products Thereof, *J. Org. Chem.*, 63(7), 1998, 2072-2085.
 21. Kavala V and Patel B K. Reinvestigation of the Mechanism of gem-Diacylation: Chemoselective Conversion of Aldehydes to Various gem-Diacylates and Their Cleavage under Acidic and Basic Conditions, *Eur. J. Org. Chem.*, 2005(2), 2005, 441-451.
 22. Gopinath R and B K Patel. Tetrabutylammonium Tribromide (TBATB)-MeOH: An Efficient Chemoselective Reagent for the Cleavage of tert-Butyldimethylsilyl (TBDMS) Ethers, *Org. Lett.*, 2(26), 2000, 4177-4180.
 23. Manju Baghmar, Pradeep K. Sharma. Kinetics and mechanism of the oxidation of aliphatic aldehydes by tetrabutylammonium tribromide, *International Journal of Chemical Kinetics, John Wiley and Sons, Inc.*, 33(6), 2001, 390-395.
 24. Manju Baghmar, Pradeep K. Sharma. Kinetics and mechanism of the oxidation of α -hydroxy acids by tetrabutylammonium tribromide, *Ind. Jour. Chem.*, 40A(3), 2001, 311-315.
 25. Ashok Kumar, Kirti Chaudhary, Pradeep K. Sharma, Kalyan K. Banerji. Kinetics and mechanism of the oxidative regeneration of carbonyl compounds from oximes by tetrabutylammonium tribromide, *Ind. Jour. of Chem.*, 40A(3), 2001, 252-255.
 26. Jaya Gosain, Pradeep Sharma. Kinetics and mechanism of the oxidation of formic and oxalic acids by tetrabutylammonium tribromide, *Ind. Jour. of Chem.*, 41A(2), 2002, 321-324.
 27. Zende S N, Kalantre V A and Gokavi G S. Kinetics and mechanism of oxidation of dimethyl and diphenyl sulfoxides by tetrabutylammonium tribromide, *J. Sulfer Chem.*, 29(2), 2008, 171-178.

28. Sharma P K. Kinetics and mechanism of oxidation of lower oxyacids of phosphorus by tetrabutylammonium tribromide, *Indian J. Chem*, 41A(8), 2002, 1612-1615.
29. Kalantre V A and Gokavi G S. Oxidation of tellurium (IV) by tetrabutyl- ammonium tribromide, *Indian J. Chem*, 44A(10), 2005, 2048-2050.
30. Kalantre V A and Gokavi G S. "Kinetics and mechanism of oxidation by selenium (IV) by tetrabutyl ammonium tribromide" *Oxidation Commun*, 29(2), 2006, 385-391.
31. Kalantre V A, Mardur S P and Gokavi G S. Kinetics and mechanism of vanadium (IV) oxidation by tetrabutylammonium tribromide, *Trans. Met. Chem*, 32(2), 2007, 214-218.
32. Thombare M R and Gokavi G S. Oxidative bromination of acetophenones by Oxone in presence of bromide ion: Kinetic and mechanistic study, *Journal of Shivaji University (Science and Technology)*, 42(1), 2016-17, 1-9.
33. Bhagwansing Dobhal, Ravindra Shimpi, Mazahar Farooqui, Sandipsing Gour and Milind Ubale, Kinetics of permagnetic oxidation of 4-hydroxy acetophenone in acidic media, *Derpharma Chemica*, 7(10), 2015, 304-308.
34. Kothoff I M, Meehan E J and Carr E M. Mechanism of Initiation of Emulsion Polymerization by Persulfate¹, *J. Am. Chem. Soc*, 75(6), 1953, 1439-1441.
35. Mahesh R T, Bellakki M B and Nandibewoor S T. Spectral and Mechanistic Study of the Ruthenium(III) Catalysed Oxidation of Gabapentin (Neurontin) by Heptavalent Manganese: A Free Radical Intervention, *Catal. Lett*, 97(1-2), 2004, 91-98.
36. Nath M P and Banerji K K. Kinetics and mechanisms of the oxidation of methyl aryl ketones by acid permanganate, *Aust. J. Chem*, 29(9), 1976, 1939-1945.
37. Yeljair Monascal, Eliana Gallardo, Loretta Cartaya, Alexis Maldonado, Yenner Bentarcurt and Gabriel Chuchani. The keto-enol equilibrium and thermal conversion kinetics of 2- and 4-hydroxyacetophenone in the gas phase: a DFT study, *MOLECULAR PHYSICS, An International Journal at the Interface Between Chemistry and Physics*, 116(2), 2017, 194-203.

Please cite this article in press as: Ravindra Shimpi. Kinetic study of oxidation of 4-hydroxy acetophenone by tetrabutyl ammonium tribromide in acidic media, *Asian Journal of Research in Chemistry and Pharmaceutical Sciences*, 6(4), 2018, 233-241.