



OXIDATIVE KINETICS OF PRENYLATED CHALCONES BY N-BROMO ACETAMIDE IN ACID MEDIUM

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ABSTRACT

The kinetic results of the oxidation of chalcones, namely, (E)-1-(4-(3-methyl but-2-enyloxy)-2-hydroxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one, (E)-1-(4-(3-methyl but-2-enyloxy)-2-hydroxyphenyl)-3-p-tolyl prop-2-en-1-one, (E)-1-(4-(3-methyl but-2-enyloxy)-2-hydroxyphenyl)-3-phenyl prop-2-en-1-one, (E)-1-(4-(3-methyl but-2-enyloxy)-2-hydroxyphenyl)-3-(4-chloro phenyl)prop-2-en-1-one, (E)-1-(4-(3-methyl but-2-enyloxy)-2-hydroxyphenyl)-3-(3-nitro phenyl)prop-2-en-1-one, by N-bromo acetamide in 70% (V/v) acetic acid - water-perchloric acid medium at various temperatures. It is noticed that the reaction is first order in [NBA] and fractional order in [chalcones] and [H⁺]. The reaction is inhibited by the addition of acetamide. The rate of oxidation is susceptible to change in the composition of acetic acid - water mixture. The negative value of ρ (reaction constant) indicates the reaction is facilitated by high electron density at the reaction site. The relative rates of oxidation, activation parameters and substituent effects have been used to suggest the plausible mechanisms of reactions.

Keywords: 4'-prenyloxy, 2'-hydroxychalcone, derivatives, oxidation

INTRODUCTION

N-Bromo acetamide (NBA) has been used as oxidizing and halogenating agent¹ in quantitative estimation of a large number of compounds. Various investigations on oxidation kinetics involving NBA and primary alcohols², aminoacid³, ketones⁴⁻⁸ and dimethyl sulfoxide⁹, Carbohydrate¹⁰, hydroxyl acid¹¹⁻¹² in acidic or alkaline media have been reported. Various oxidants have been used for the oxidation of unsubstituted and substituted phenyl styryl ketones (PSK and SPSK respectively) i.e. chalcones¹³⁻¹⁹. Phenyl styryl ketones undergo oxidation which is amenable to kinetic investigation. PSK contains two functional groups >C=C< and >C=O, and in order to ascertain the actual site attack by the oxidant, kinetics of oxidation of PSK having substituents in the phenyl rings has been under taken. For lack of information on similar studies using N-bromoacetamide (NBA) as an oxidant, the kinetic study has been taken up with a view to finding out the reactive species and mechanism of reaction.

EXPERIMENTAL

Materials

All chemicals used were of either E.merck or lancast grade and further purification was made by recrystallization or distillation. NBA was prepared by reported method²⁰ and its purity was checked with IR, NMR and also by iodometric determination of active bromine present. PSKs were prepared by Claisen Schmidt condensation of corresponding substituted benzaldehydes and 2-hydroxy acetophenone in the presence of aq.KOH and ethanol and purified by column chromatography²¹ and checked with IR, ¹H NMR ¹³C NMR, and MASS. Acetic acid (AR, BDH) was purified by standard method²². Conductivity water was used.

Kinetic Measurements

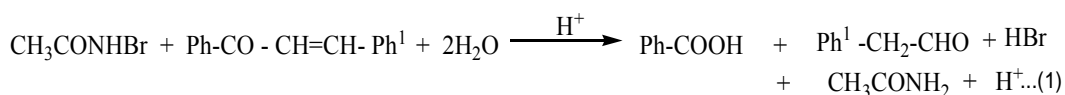
The reaction was carried out under pseudo-first order conditions by keeping an excess (10x greater) of the [PSK] over [NBA] in blackened flasks to avoid any photochemical reaction. Aliquots were withdrawn at suitable time intervals and the amount of unreacted NBA was determined by iodometric titrations up to completion of 70% of the reaction. Rate constants were computed from the linear plots of log [NBA] versus time. Duplicate kinetic runs showed that the data were reproducible within $\pm 3\%$.

Stoichiometry

The stoichiometry of the reaction was determined by carrying out several sets of experiments with varying amounts of NBA largely in excess over chalcone. The estimation of unreacted NBA showed that one mole of each chalcone reacts with one mole of NBA.

Product analysis

The product analysis was done under kinetic conditions. PSK (0.01 mol) and NBA (0.01 mol) were made up to 50 ml in perchloric acid (0.5M) and kept in dark for 24 hrs till the completion of oxidation. One mole of NBA reacts with one mole of chalcone giving rise to corresponding benzoic acid and phenyl acetaldehyde as per the (eq.1). The products of oxidation were identified as benzoic acid and phenyl acetaldehyde. Benzoic acid and Phenyl acetaldehyde were detected by TLC and compared with those of the authentic samples. The presence of Phenyl acetaldehyde among the reaction product was also detected by preparing their 2,4-dinitrophenyl hydrazone derivatives.



RESULTS AND DISCUSSION

Effect of N-bromoacetamide.

The kinetics of oxidation of chalcones has been studied at various initial concentrations of the oxidant [NBA] (0.001M to 0.01M) and at fixed concentrations of other reactants. The plot of log (a-x) versus time yields a straight line ($r = 0.998$) with negative slope. The pseudo-first-order rate constants, k_{obs} which are calculated from these slopes, at various initial concentrations of the oxidant, are constant indicating a first order dependence of rate on NBA (**table-1**) in 70-30% acetic acid-water mixture in the presence of perchloric acid.

Effect of substrate

The kinetic investigation has been made at various concentration of substrate (0.002 to 0.02M) and at fixed [NBA], $[\text{H}^+]$. The Plots of log k_{obs} versus log [chalcone] are linear ($r = 0.9995$) with a slope of less than unity (0.45-0.55) for all the substrates indicating a fractional order dependence on [substrate]. A definite intercept was obtained with $1/k_{\text{obs}}$ versus $1/[\text{chalcone}]$, indicating the formation of a complex between oxidant and substrate.

Effect of perchloric acid

The kinetic investigation has been made at various concentrations of perchloric acid (0.002M to 0.02M) and at fixed [NBA], [substrate]. Observed rate constants increase with increases in $[\text{HClO}_4]$ in the range (0.2-2.0) mol.dm⁻³ (**table-1**). Plots of log k_{obs} versus log [perchloric acid] are linear ($r = 0.998$) with a slope of less than unity (0.45-0.56) for all the substrates indicating a fractional order in perchloric acid.

Effect of acetic acid

The effect of dielectric constant on the rate of reaction has been studied by varying the percentage of acetic acid in the reaction mixture from 50% to 70% for the reaction carried out in acidic medium. The rate decreases with increase in dielectric constant of the medium and the results are recorded in (**table-4**) the plot of log k_{obs} against $1/D$ (where D is the dielectric constant of the medium) use a straight line with negative slope indicating dipole-dipole interaction. Added salts like KCl, NaClO₄ do not have any effect on the rate.

Effect of acetamide

A variation in [acetamide] has been employed in these reactions with a view to find the reactive species of the oxidant. The results indicate that the rate decreases with an increase in the concentration of acetamide. For example k_{obs} for chalcone from 2.107×10^{-3} to $0.46 \times 10^{-3} \text{sec}^{-1}$, when the acetamide is changed from 0.004 M to 0.02 M. The plot of $\log k_{\text{obs}}$ versus $\log [\text{acetamide}]$ yields a straight line ($r = 0.998$) with negative slope.

Effect of temperature

The reactions have been studied in the temperature range 288-308K and the results are recorded in **(table-2)**. Using Arrhenius equation the energy of activation for each substrate has been calculated from the slope of the straight line ($r = 0.998$) obtained by plotting $\log k_{\text{obs}}$ against $1/T$. This value has been subsequently utilized in computing various other thermodynamic parameters and all the results are presented in **(table-3)**.

Effect of substituent

The effect of substituent on the rate was studied by taking prenylated chalcone and four substituted chalcones and the reactivities followed the order; $p\text{-OCH}_3 > p\text{-CH}_3 > p\text{-H} > p\text{-Cl} > m\text{-NO}_2$, **(table-1)**. It is clear that electron releasing groups increase the rate and vice versa. The plot of $\log k_{\text{obr}}$ versus σ gave a straight line with negative slope of 0.45 to 0.55.

The oxidation of prenylated chalcones by NBA under nitrogen atmosphere fails to induce polymerization of added acrylonitrile, thus ruling out radical oxidation.

The retarding effect of added acetamide suggests that the pre-equilibrium step involves hydrolysis of NBA to give acetamide and HOBr **(eq .2)**.



Under strongly acidic condition the possibility of H_2OBr^+ from HOBr is remote since carbonyl oxygen of the substrate with α, β -unsaturated system to back up gets protonated with relative ease. The mechanism proposed involves the attack of HOBr on the carbonyl carbon with simultaneous release of H^+ . The cleavage of C-C bond on account of the propensity of bromine to leave as anion is aided by the attack of H_2O molecule on the vinylic carbon adjacent to the carbonyl system. The enol resulted with the formation of HBr undergoes tautomerism to yield phenylacetaldehyde.

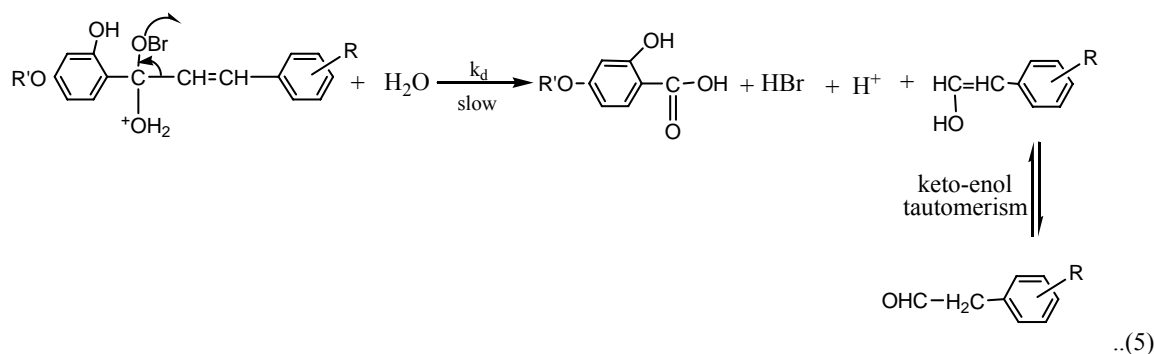
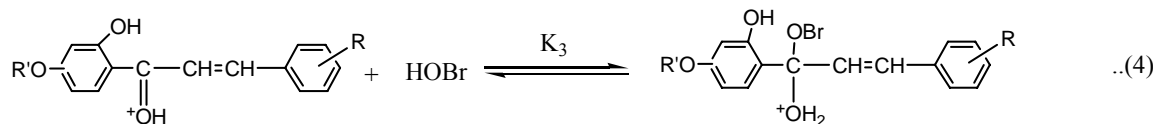
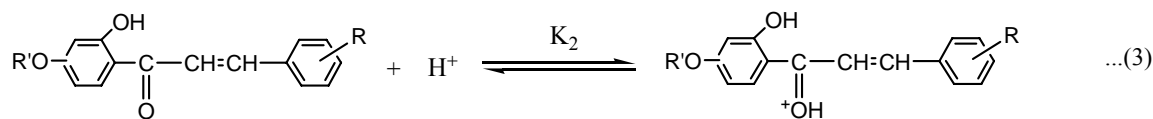
The rate law based on **scheme-1** is represented by **eq - 6**.

$$\frac{-d[\text{NBA}]}{dt} = \frac{k_d K_1 K_2 K_3 [\text{NBA}] [\text{Chalcone}] [\text{H}^+]}{[\text{CH}_3\text{CONH}_2] + K_1 + K_1 K_2 K_3 [\text{Chalcone}] [\text{H}^+]} \quad \dots(6)$$

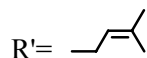
The observed results clearly points out that the reaction is first order in [NBA], fractional order in [chalcones] and $[\text{H}^+]$ and inverse order in [acetamide] which is also supported by the active thermodynamic parameters. The activation energy value is the highest for the slowest reaction and vice versa. Constancy of ΔG^\ddagger values calculated for all the chalcones indicates that probably the same mechanism prevails in all the cases. The negative values for entropy of activation reflect that the activated complex is more rigid. The rate of reaction increased with the presence of electron releasing group in the phenyl ring of aldehydic part of the chalcone. It is understandable from the electron deficiency prevailing around reaction site. The protonated hydroxyl leaving of bromide ion and the heterolytic cleavage of the C-C bond encouraged by the attack of H_2O .

ACKNOWLEDGEMENTS

The authors thank the principal and management, KITS, warangal for providing necessary facilities and encouragement and one of the authors (N.B) thank APCOST, Hyderabad, (AP). for the award of young scientist fellowship.



R= p-OCH₃, p-CH₃, p-H, p-Cl, m-NO₂



Scheme-1

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Table-1:Effect of varying [reactants] on the rate constants
[Hg (OAc)₂] = 0.002 mol dm⁻³; Solvent; water-acetic acid(30-70%, v/v); Temp = 293K]

10 ² .[NBA] mol.dm ⁻³	10 ² .[Sub] mol.dm ⁻³	[H ⁺] mol.dm ⁻³	k _{obs} x 10 ³ (s ⁻¹).				
			p-OCH ₃	p-CH ₃	p-H	p-Cl	m-NO ₂
0.1	1.0	0.5	4.490	3.799	3.461	2.759	1.458
0.25	1.0	0.5	4.388	3.740	3.475	2.673	1.433
0.5	1.0	0.5	4.417	3.641	3.552	2.662	1.538
0.75	1.0	0.5	4.459	3.717	3.410	2.707	1.458
1.0	1.0	0.5	4.374	3.637	3.556	2.738	1.403
0.1	0.2	0.5	2.303	1.995	1.589	1.381	0.575
0.1	0.5	0.5	3.684	2.763	2.686	2.226	1.036
0.1	1.0	0.5	4.490	3.799	3.461	2.759	1.458
0.1	1.5	0.5	5.450	5.258	4.132	3.224	1.919
0.1	2.0	0.5	6.750	6.179	5.642	4.337	2.610
0.1	1.0	0.2	2.629	2.454	2.051	1.437	1.236
0.1	1.0	0.5	4.490	3.799	3.461	2.759	1.458
0.1	1.0	1.0	5.339	5.293	3.730	3.006	1.945
0.1	1.0	1.5	7.098	6.090	4.800	4.347	2.878
0.1	1.0	2.0	9.456	7.655	6.512	4.911	3.085

Table-2:Effect of temperature on the rate constant [Hg (OAc)₂] = 0.002 mol.dm⁻³;
[chalcones] = 0.01mol dm⁻³; [NBA] = 0.001 mol dm⁻³, [Solvent; water-acetic acid]
(30-70%v/v); Temp = [288-308K]

T	k _{obs} x 10 ³ (s ⁻¹)				
	p-OCH ₃	p-CH ₃	p-H	p-Cl	m-NO ₂
288	3.898	3.081	2.528	1.976	1.038
293	4.490	3.799	3.461	2.759	1.458
298	6.368	4.467	4.261	3.512	1.985
303	7.749	5.628	5.364	4.441	2.553
308	9.155	7.923	7.019	5.727	3.337

Table-3:Activation parameters for the oxidation of chalcones by NBA in acid Medium [chalcone] = 0.01mol dm⁻³; [NBA] = 0.001 mol dm⁻³; [Hg (OAc)₂] = 0.002 mol dm⁻³; T_{amp} =293K.

Parameters	p-OCH ₃	p-CH ₃	p-H	p-Cl	m-NO ₂
E _a (k.J)	31.44	33.76	36.32	38.15	42.43
ΔH [‡] (k.J)	29.00	30.93	33.87	35.70	39.99
-ΔS [‡] (Jk ⁻¹ mol ⁻¹)	190.77	192.16	193.04	194.82	200.13
ΔG [‡] (k J.mol ⁻¹)	84.89	89.68	90.43	92.79	98.63

Table-4:Effect of acetic acid on the rate constant $[\text{Hg}(\text{OAc})_2] = 0.002 \text{ mol dm}^{-3}$; $[\text{chalcone}] = 0.01 \text{ mol dm}^{-3}$; $[\text{NBA}] = 0.001 \text{ mol dm}^{-3}$; $[\text{Solvent; Acetic acid}](50\text{-}70\%, \text{v/v})$; $\text{Temp} = 293\text{K}$.

S. No	Acetic acid %	$k_{\text{obs}} \times 10^3 (\text{s}^{-1})$				
		p-OCH ₃	p-CH ₃	p-H	p-Cl	m-NO ₂
1	50	13.688	9.938	7.679	4.534	2.837
2	55	11.692	8.234	6.486	3.969	2.471
3	60	9.876	7.029	5.483	3.339	2.131
4	65	7.677	5.444	4.285	2.708	1.745
5	70	6.171	4.222	3.465	2.164	1.473

(Received:1 December 2008

Accepted: 28 December 2008

RJC-295)

“The difference between the right word and the almost right word is the difference between lightning and a lightning bug.”

- Mark Twain