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Kinetic Screening and Mechanistic Investigations of Oxygenation of 5-Oxo Acids by N-Bromosuccinimide in Acid Medium

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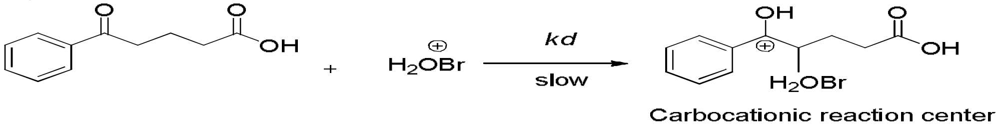
ABSTRACT

The kinetics and mechanistic investigation of oxidation of substituted 5-oxo-5-phenylpentanoic acids (commonly known as 5-oxo acids) by N-bromosuccinimide (NBS) has been studied in aqueous acetic acid medium. The reaction follows first order dependence in [NBS], [H_2SO_4] and [5-oxoacid]. Decrease in the dielectric constant of the solvent enhanced the rate of reaction. Variation of ionic strength does not influence the rate and reaction failed to induce polymerization of added acrylonitrile. Oxygenation rate is accelerated by the presence of electron-donating substituents on the phenyl ring of 5-oxo acids and is retarded by the electron-withdrawing substituents. The linear free energy relationship is characterized by the linearity in Hammett plots of log k against σ. The reaction constant is negative and decreases with increase in temperature. Isokinetic relationship is discussed from the intersection lines of Arrhenius and Hammett plots. The mechanism proposed involves the attack of protonated species of N-bromosuccinimide (H_2O^+Br) on the enol form of 5-oxo acids forming a carbocationic reaction center, which by carbon-carbon bond cleavage yield the corresponding benzoic acids in the fast step. The reaction is an example of neighboring group participation in intramolecular catalysis and is potentially useful for the regioselective synthesis of substituted benzoic acids in quantitative yields.

GRAPHICAL ABSTRACT

The kinetics and mechanistic investigation of oxidation of substituted 5-oxo-5-phenylpentanoic acids (commonly known as 5-oxo acids) by N-bromosuccinimide (NBS) has been studied in aqueous acetic acid medium. The reaction follows first order dependence in [NBS], [H_2SO_4] and [5-oxoacid].The linear free energy relationship is characterized by the linearity in Hammett plot of log *k* against σ. The mechanism proposed involves the attack of protonated species of N-bromosuccinimide (H_2O^+Br) on the enol form of 5-oxo acids forming a carbocationic reaction center, which by carbon-carbon bond cleavage yield the corresponding benzoic acids in the fast step.



Keywords: 5-Oxoacids, N-Bromosuccinimide, Kinetics, Isokinetic Relationship.

INTRODUCTION

5-oxo-5-arylpentanoic acids (commonly known as 5-oxo acids or δ – oxo acids) have much biological significance and play an essential role in pharmaceutical chemistry as anti-rheumatic agents and adjuvant arthritis suppressing agents. Among the various organic compounds employed in oxidation studies, 5-oxo acids are attractive substrates in terms of their chemical structures. The carbonyl and carboxy groups of 5-oxo acids are separated by three carbon atoms, hence, the two functional groups are essentially independent and they behave both as oxo compounds as well as acids without the direct influence of other group [1-3]. Among the various organic compounds employed in these studies, 5-oxo acid is an attractive substrate in terms of its enolization in strong acid medium and the enol form is reported to be the reactive species [4, 5] in its reactions with many oxidants.

N-bromosuccinimide (NBS) is a source of positive halogen and this reagent has been exploited as oxidant for a variety of substrates in both acidic and alkaline medium [6]. The nature of active oxidizing species and the mechanism depends on the nature of the halogen atom, the groups attached to the nitrogen and the reaction condition. The species responsible for such oxidizing character may be different depending on the *p*H of the medium. The probable reactive species [7] of NBS in acid solution are >NX, HOX, > N^+HX, or H_2OX^+ and the reactive species in alkaline solutions are >NH, HOX and OX^-.

In recent years, studies of oxidation of organic compounds by N-halo compounds in the presence of acid have attracted considerable attention [8]. A thorough literature survey reveals that only few works on the oxidation of 5-oxo acids (**S**) have been reported [9, 10]. Although the N-bromosuccinimide oxidation of a large variety of organic compounds has been studied, there seems to be no report on a systematic kinetic study of the oxidation of 5-oxo acids by N-bromosuccinimide.

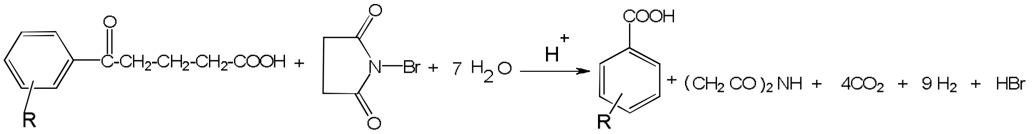
As a part of our ongoing research and in continuation of earlier work, the author herein reports the kinetics and mechanistic investigation of oxidation of 5-oxo acids using N-Bromosuccinimide. The oxidation of 5-oxo acids has been studied to ascertain the reactive species of substrate and oxidant, elucidate a plausible mechanism, deduce an appropriate rate law, identify the reaction products and evaluate the kinetic and thermodynamic parameters.

MATERIALS AND METHODS

Materials: The substrates 5-oxo -5- phenyl pentanoic acid (5-oxo acid) and phenyl substituted 5-oxo acids were prepared from Friedel-Crafts acylation of substituted benzene with glutaric anhydride [11-15]. Nitration of oxo acids has been performed under mild conditions to prepare nitro compounds. All the 5-oxoacids were crystallized twice from water and their purity was checked by their melting points and UV, IR and NMR spectra. All other chemicals were of analytical grade; H_2SO_4 and mercuric acetate (E. Merck) were used as received. Acetic acid (BDH) was purified by refluxing over chromic acid for 6h and then distilled. The other solutions were prepared with either doubly distilled water or purified acetic acid and were used for each kinetic run. A Schimadsu multipurpose recording double beam UV-visible spectrophotometer equipped with a temperature controller was used for absorption studies. Separation and identification of organic intermediates in the reaction were performed using high performance liquid chromatography (HPLC). The experiments were performed with Schimadsu equipment using an ion-exchange column at 45º C and a UV detector working at 220 nm. The intermediates and the products were identified from their retention time (t_r). Regression analyses of experimental data yielded the regression coefficient (r) and standard deviation (s).

Kinetic measurements: A thermostatic water bath was used to maintain the desired temperature within ± 0.1º C. The kinetic measurements were carried out in black-coated vessels at constant temperature (± 0.1º C) and performed under pseudo-first order conditions with [oxo acid] >> [NBS]. The reaction mixture containing 5-oxo acid, sulphuric acid and mercuric acetate was equilibrated for an hour at desired temperature under subdued light. The reaction was initiated by the addition of temperature-equilibrated NBS solution of required concentration. The progress of the reaction was monitored iodometrically by estimating the unreacted NBS. However, before adopting Iodometric method, it was ensured that the presence of 5-oxo acids in the quenching solution of potassium iodide did not change the NBS titer value. The course of the reaction was followed, upto 90% completion, by monitoring NBS concentration and the pseudo-first order rate constants (k, s^{-1}) were computed from the linear plots of log $[NBS]_t$ against time and the rate constants were reproducible within ±5%. Rate constants did not alter in a nitrogen atmosphere and all the rate constants reported were obtained without nitrogen. Freshly prepared solutions of oxo acids in purified acetic acid were used to avoid any possible side-reactions. In order to keep back all the bromide ions formed, an optimum concentration (0.005 $mol.dm^{-3}$) of $Hg(OAc)_2$ has been employed. Hence, the reported rate constants and thermodynamic parameters pertain to pure NBS (uncontaminated with Br_2) oxidation only.

Stoichiometry and product analysis The stoichiometry of the reaction was determined by equilibrating different sets of reaction mixtures containing an excess of [NBS] over [5-oxo acid] at 40 ºC for 24 h, keeping all other reagents constant in an inert atmosphere. Estimation of unconsumed NBS concentration revealed that one mole of oxo acid required one mole of N-bromosuccinimide for oxidation.



(1)

The same stoichiometry was observed with all the substituted 5-oxo acids. The ultimate product of oxidation of 5-oxo acid are benzoic acids, identified by the retention time of the authentic samples. Benzoic acid after separation by HPLC, was estimated quantitatively (92–96% yield) with a standard curve by its absorption at 235nm (λ_{max}). CO_2 was identified by bubbling N_2 gas through a U-shaped tube containing a saturated $Ba(OH)_2$ solution. Formation of white precipitate of $BaCO_3$ indicated the liberation of CO_2.

RESULTS AND DISCUSSION

Role of mercuric acetate Mercury (II) can act as a homogeneous catalyst, co-catalyst and oxidant [16, 17]. In the present study, mercury (II) acetate has been used as a scavenger to fix up Br^- ions formed in the course as $HgBr_2$ or $HgBr_4^{2-}$. An optimum concentration (0.005 mol dm^{-3}) of mercuric acetate was employed to keep back all the formed bromide ions. The added mercuric acetate over a wide concentration range (0.001–0.01 mol dm^{-3}) had no effect on the rate of reaction. Hence, the added Hg(II) ion is therefore to eliminate bromide ion in the reaction without perturbing the kinetic results.

Kinetic results and effect of concentration of reactants At fixed concentrations of acid, $Hg(OAc)_2$ and when [oxo acid] is in 10-fold excess over [NBS], the disappearance rate of [NBS] followed first-order rate law as was observed from the linear plots of log $[NBS]_t$ versus time ($R^2 \geq 0.99$) for more than three half-lives of the reaction. Further, the pseudo-first order rate constant (k, s^{-1}), evaluated from the slopes of such plots remained unchanged (Table 1) with the variation of $[NBS]_o$, confirming the first order dependence of the rate on $[NBS]_o$.

Table 1: Dependence of rate on the factors influencing the oxidation of 5-oxo acids by N-bromosuccinimide in acidic medium at 313 K

10^3 [NBS] (mol dm^{-3})	10^2 [5-oxo acid] (mol dm^{-3})	[H$^+$] (mol dm^{-3})	AcOH-H$_2$O ^{b} v)	10^4 k (s^{-1}) ^{a}				
				-H	*p*-OCH$_3$	*p*-CH$_3$	*p*-Cl	*m*-NO$_2$
0.5	1.0	1.0	50-50	3.73	9.57	5.76	1.24	0.34
1.0	1.0	1.0	50-50	3.74	9.59	5.75	1.25	0.33
1.5	1.0	1.0	50-50	3.72	9.58	5.74	1.27	0.35
2.0	1.0	1.0	50-50	3.72	9.59	5.76	1.27	0.32
3.0	1.0	1.0	50-50	3.72	9.59	5.75	1.28	0.35
1.0	0.5	1.0	50-50	1.42	4.79	2.87	0.57	0.18
1.0	1.0	1.0	50-50	3.72	9.59	5.75	1.27	0.35
1.0	2.0	1.0	50-50	6.24	18.22	10.25	2.52	0.57
1.0	3.0	1.0	50-50	8.52	30.12	17.62	3.64	1.21
1.0	4.0	1.0	50-50	13.58	42.79	21.32	4.54	1.43
1.0	1.0	0.5	50-50	1.54	4.32	3.62	0.68	0.22
1.0	1.0	1.0	50-50	3.72	9.59	5.75	1.27	0.34
1.0	1.0	1.5	50-50	4.85	13.22	9.63	2.15	0.49
1.0	1.0	2.0	50-50	6.72	18.62	11.42	2.55	0.72
1.0	1.0	2.5	50-50	9.32	24.12	16.20	3.68	0.85
1.0	1.0	3.0	50-50	12.58	31.45	19.54	5.84	1.21
1.0	1.0	1.0	30-70 (3.18)*	1.15	3.73	2.34	0.42	0.16
1.0	1.0	1.0	40-60 (46.48)	2.12	5.22	3.54	0.76	0.22
1.0	1.0	1.0	50-50 (39.78)	3.72	9.59	5.75	1.27	0.35
1.0	1.0	1.0	60-40 (33.08)	5.85	17.25	8.85	2.12	0.57
1.0	1.0	1.0	70-30 (26.08)	10.52	37.24	16.24	4.11	1.27

[a] Reported rate constants are the mean of duplicate experiments.
[b] Parentheses values indicate the dielectric constant of the medium.

The effect of [oxo acid] on the reaction rate was studied in the concentration range 0.005–0.03 mol dm^{-3} at constant concentration of oxidant, acid and mercuric acetate (Table 1). The plots of log k versus log [substrate] were linear ($R^2 \geq 0.99$) with slope values equal to unity suggesting the first order dependence of rate on [oxo acid]. Further, the Michaelis-Menten plots of 1/*k* against 1/[oxo acid] were also linear passing from the origin (Fig. 1) confirming that the order in [substrate] is equal to unity.

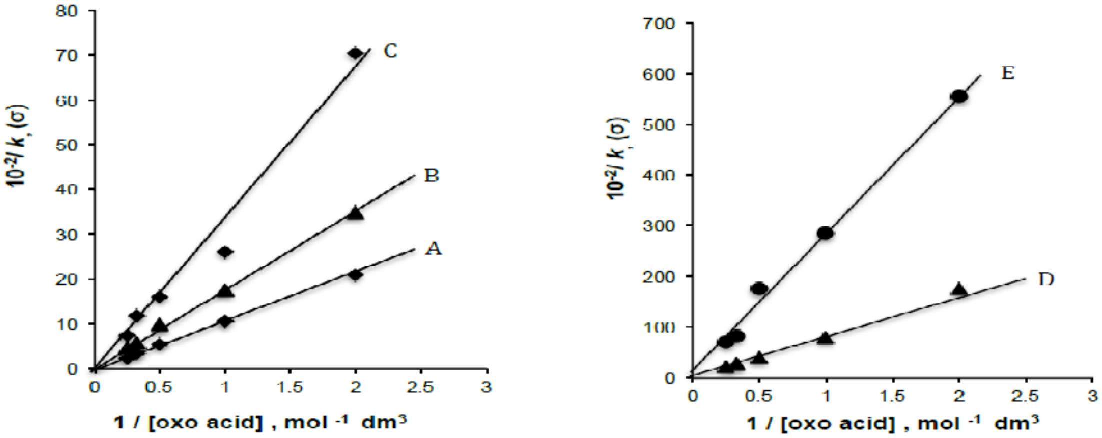


Fig 1: Representative Michaelis-Menten plots for the N-bromosuccinimide oxidation of 5-oxo acids.
A) p –OCH_3 , B) p –CH_3 , C) –H , D) p – Cl , E) m – NO_2.

The dependence of reaction rate on the concentration of acid has been investigated at different initial concentrations of sulphuric acid, keeping the concentrations of the other reactants constant. The rate of the reaction increased linearly with an increase in [H_2SO_4] (Table 1) and the order with respect to [acid] was found to be one from the linear plots of log *k* versus log [acid]. This establishes that the reaction is first order with respect to acid and a plot of *k* versus [acid] is linear (Fig. 2) passing through the origin showing that the reaction proceed through an acid-catalyzed pathway [18].

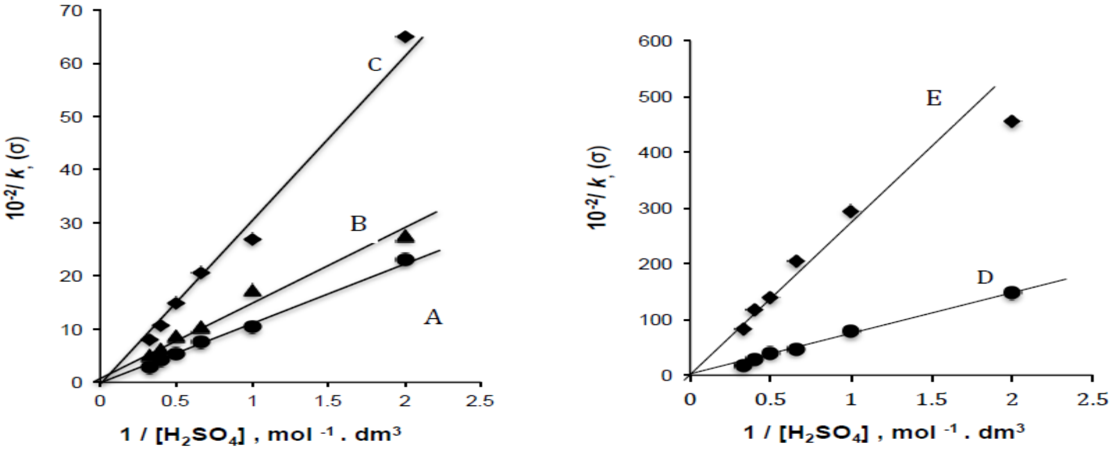


Fig 2: Plot of 1/*k* against 1/[H_2SO_4] for the N-bromosuccinimide oxidation of 5-oxo acids.
A) p –OCH_3 , B) p –CH_3 , C) –H , D) p – Cl , E) m – NO_2.

Varying acetic acid and water composition varied dielectric constant of the medium (Table 1), which favors the reaction involving protonation. The plot of log *k* versus 1/D for all the studied substrates is linear with a positive slope, indicating an interaction between a positive ion (cation) and a dipole molecule. This further supports the postulation of (H_2O^+Br) as the reactive species. Blank experiments showed that acetic acid was not oxidized by NBS under the prevailing conditions. The observed results therefore truly represent the rates under different dielectric media of the solution.

The reactions were studied in presence of added acrylonitrile/acrylamide (in N_2 medium) to examine the intervention of free radicals. There was no effect of added acrylic monomers (0.1 – 1.0 mol.dm^{-3}) on the reaction rate. Also no precipitate due to polymerization of acrylic monomer was observed, ruling out the participation of free radical intermediates in the reaction. To further confirm the absence of free radicals in the reaction pathway, reactions were carried out in the presence of 0.05 mol.dm^{-3} butylated hydroxyl toluene (BHT). The unchanged BHT was recovered almost quantitatively at the end of the experiment.

The oxidation reactions were studied in the temperature range of 298–323 K keeping all constituents of the solution constant (Table 2). Activation energy (E_a) of the reactions was calculated from the least-square slopes of linear Arrhenius plots (Fig. 3, $R^2 \geq 0.99$) of log *k* versus 1/T and the related thermodynamic parameters *viz.* enthalpy of activation ($\Delta H^{\neq}$), entropy of activation ($\Delta S^{\neq}$) and Gibbs free energy of activation ($\Delta G^{\neq}$) were calculated using appropriate equations and are presented in Table 3. The plot of $\Delta H^{\neq}$ against $\Delta S^{\neq}$ was linear (Fig. 4a; $R^2 \geq 0.999$) and the isokinetic temperature ($\mathbf{T_{iso}}$) obtained is 357.14 K. The $\mathbf{T_{iso}}$ calculated from the Exner' s plot (Fig.4b; $R^2 \geq 0.989$) of log k_{323K} against log k_{313K} is 354.52 K, which is in good agreement with the value obtained from the $\Delta H^{\neq}$ against $\Delta S^{\neq}$ plot.

Table 2: Rate constants at different temperatures and activation parameters for the N-Bromosuccinimide oxidation of 5-oxo acids in acid medium

	10^4 k (s^{-1})				
Temperature (K)	-H	*p*-OCH_3	*p*-CH_3	*p*-Cl	*m*-NO_2
303	1.52	4.58	2.78	0.29	–
308	2.87	7.87	3.45	0.57	0.15
313	3.72	9.59	5.75	1.27	0.35
318	4.42	13.81	6.82	1.73	0.83
323	9.59	17.42	7.94	3.80	1.38
Ea (kJ·mole^{-1})	64.90	52.46	57.05	110.86	146.66
$\Delta H^{\neq}$ (kJ·mole^{-1})	62.30	49.86	54.45	108.26	144.06
$\Delta S^{\neq}$ (J ·mole^{-1}·K^{-1})	-111.84	-143.72	-133.29	25.60	129.57
$\Delta G^{\neq}$ (kJ·mole^{-1})	97.31	94.84	96.25	100.17	103.50

Experimental conditions : [Substrate] =1.0 × 10^{-2} mol·dm^{-3}, [$KBrO_3$] = 1.0 × 10^{-3} mol·dm^{-3}, [H_2SO_4] = 1.0 mol·dm^{-3}, [Hg $(OAc)_2$] = 5.0 × 10^{-3} mol·dm^{-3}, AcOH–H_2O = 50:50 (%, v/v).
The average error in values of *Ea*, $\Delta H^{\neq}$, $\Delta S^{\neq}$ and $\Delta G^{\neq}$ are ± 1.6 kJ·mol^{-1}, ± 1.6 kJ·mol^{-1}, ± 3 J. mol^{-1}·K^{-1} and ± 2 kJ·mol^{-1} respectively. $\Delta H^{\neq}$, $\Delta S^{\neq}$ and $\Delta G^{\neq}$ values were obtained at 313 K. The average error in rate constant is ± 5 %.

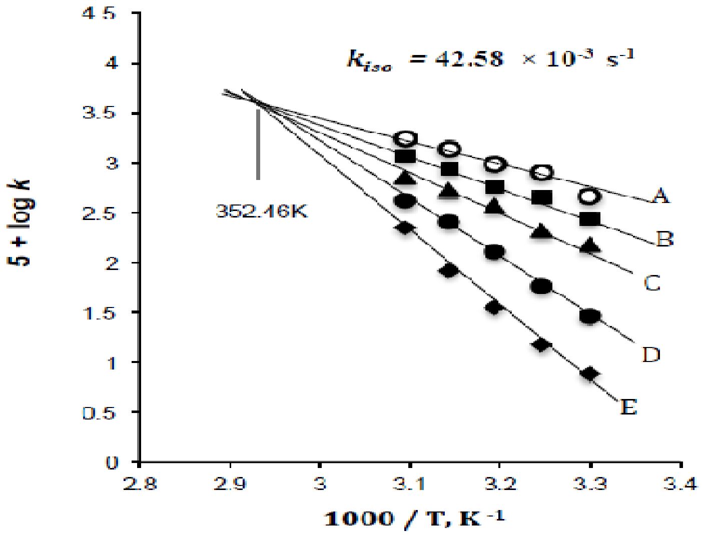


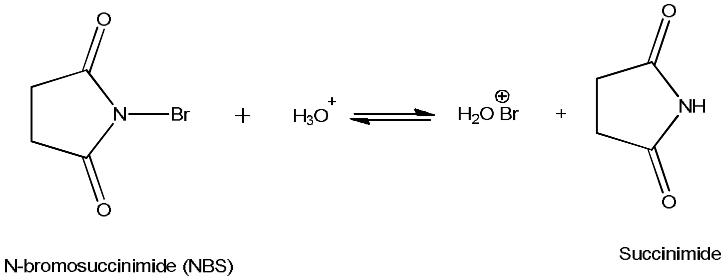
Fig 3: Arrhenius plots of log *k* versus 1/T, showing the isokinetic temperature.
A) *p* – OCH_3 , B) *p* – CH_3 , C) –H , D) *p* – Cl , E) *m* – NO_2.

The effect of substituents on the reaction rate has been studied by structural modifications in the phenyl moiety of 5-oxo acids using different phenyl substituted 5-oxo acids ($ArCOCH_2CH_2CH_2COOH$, where Ar = 4-methoxy, 4-methyl, 4-phenyl, 4-chloro, and 3-nitro respectively) at different temperatures. The electron-donating substituents enhanced the reaction rate whereas the electron-withdrawing (electron attractors) substituents retarded the rate, though perceptible, not very much. The linear free energy relationship is characterized by linearity in the Hammett plot of log *k* versus σ at all the studied temperatures (Fig. 5) with a decreasing value of Hammett reaction constant, ρ (in magnitude) by an increase of temperature from 303K – 323K. The Hammett's reaction constant is negative and is in the order of –0.89, –1.22, –1.46, –1.75 and –1.86 at 323, 318, 313, 308 and 303K respectively.

Reactive species and mechanism The role of NBS as an oxidant has been discussed in the reported oxidation of acetophenone [19], amino acids [20] and 4-oxo acids [1] in acid medium. The reports indicate that N-bromosuccinimide exist in acidic medium in the form of following equilibria

$$HOBr + H_3O^+ \rightleftarrows H_2OBr^+ + H_2O \qquad (2)$$

Thus, the most probable oxidizing species is hypobromous acidium ion (H_2O^+Br), which is a strong electrophile and oxidant, and the participation of hypohalous acidium ion is evident in many electrophilic substitution and oxidation reactions [21]. The retardation of reaction rate on the addition of succinimide suggests [22] a pre-equilibrium step which involves a process in which succinimide is one of the products.



The linear plot of inverse of the rate constant (r = 0.989) against [succinimide] suggested the involvement of the above equilibrium in the oxidation process. Similar conclusions have been arrived at in the N-chloronicotinamide [23] oxidation of amino acids, and N-bromoacetamide oxidation of some α-hydroxy acids.

5-oxo acids are weak acids with *p*Ka of about 5-6 in aqueous solutions at 40 ºC [24]. Hence, in acid medium, 5-oxo acids will exist in undissociated form. Therefore, 5-oxo acids enolize in acid medium to form the enol and proceed by a concerted or push-pull mechanism (Eqs. 4, 5). Generally, the oxidation of ketones proceeds [25] *via* enolization of the keto group and is facilitated by lowering of dielectric constant of solvent medium [26]. The rate enhancement observed in the present study with increase in the acetic acid medium establishes the involvement of the enol-form of the oxo acid in the reaction. In the present investigation, the rate of enolization (measured by the bromination method [27], under identical experimental conditions) is greater than the rate of oxidation by a factor of ~12– 15 and the enolization step can be visualized as proceeding *via* the enol-form of 5-oxo acid. Hence, the step involving enol formation can be assumed to be a fast step and thus is not the rate-determining step of the reaction. In light of these considerations, the mechanism as shown in Scheme 1 is proposed for the N-bromosuccinimde oxidation of 5-oxo acids.

The mechanistic pathway is demonstrated by (i) the formation of the active species of N-bromosuccinimide (ii) the enolization of 5-oxo acid in the presence of acid (iii) the attack of H_2O^+Br on the enol form of substrate in the rate-determining step as seen in Scheme 1 which is in accordance with the observed stoichiometry.

Derivation of rate law: Based on the mechanism (Scheme 1), the rate in terms of decrease in [NBS] can be expressed as Eq. (8).

$$\text{Rate} = \frac{-\mathrm{d[NBS]}}{\mathrm{dt}} = k_d[\text{Enol}][\mathrm{H_2O^+Br}] \qquad (8)$$

On applying steady state approximation for [Enol]

$$\text{Rate} = \frac{-\mathrm{d[NBS]}}{\mathrm{dt}} = \frac{k_2k_3k_d[\text{Oxo acid}][\mathrm{H_3O^+}][\,\mathrm{H_2O^+}Br]}{k_{-2}k_{-3}[\mathrm{H_3O^+}]+k_4(k_{-2}+k_3)[\,\mathrm{H_2O^+}Br]} \qquad (9)$$

At low $[H_3O^+]$; $k_{-2}k_{-3}[\mathrm{H_3O^+}] \gg k_d(k_{-2} + k_3)[\,\mathrm{H_2O^+}Br]$, Eq. (9) changes into

$$\frac{-\mathrm{d[NBS]}}{\mathrm{dt}} = \frac{k_2k_3k_d[\text{Oxo acid}][\mathrm{H_3O^+}][\,\mathrm{H_2O^+}Br]}{k_{-2}k_{-3}[\mathrm{H_3O^+}]} = \frac{k_2k_3k_d[\text{Oxo acid}][\,\mathrm{H_2O^+}Br]}{k_{-2}k_{-3}} \qquad (10)$$

$$\text{but,}[\mathrm{H_2O^+Br}] = k_a\frac{[\mathrm{NBS}]\,[\mathrm{H_3O^+}]}{[\text{succinimide}]} \qquad (11)$$

Therefore,

$$\frac{-\mathrm{d[NBS]}}{\mathrm{dt}} = k = \frac{k_2k_3k_dk_a[\text{Oxo acid}][\mathrm{H_3O^+}][\mathrm{NBS}]}{k_{-2}k_{-3}[\text{succinimide}]} \qquad (12)$$

$$Rate = \frac{-\mathrm{d[NBS]}}{\mathrm{dt}} = k = k_{\,obs}\frac{[\text{Oxo acid}][\mathrm{H_3O^+}][\mathrm{NBS}]}{[\text{succinimide}]} \qquad (13)$$

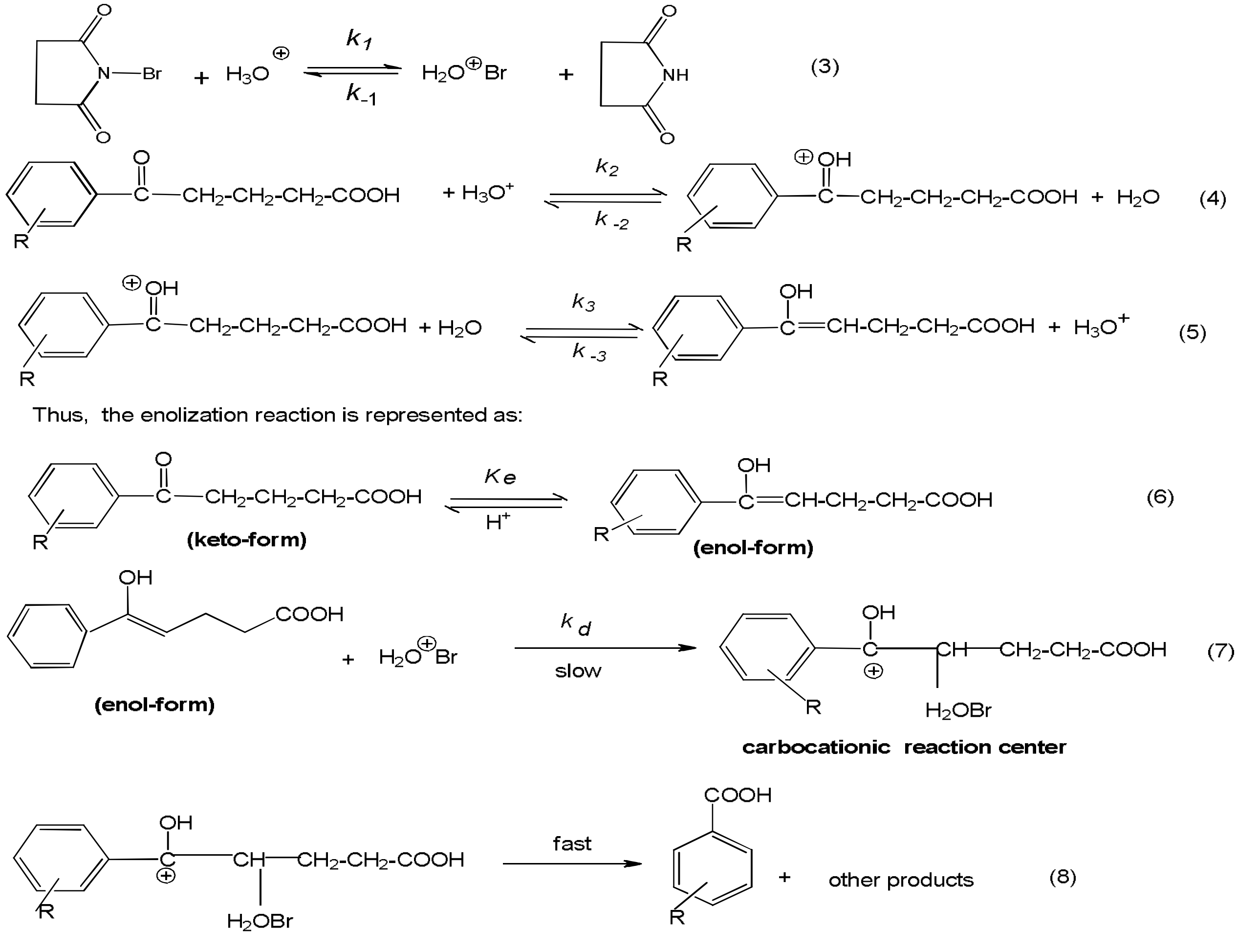
where, $k_{obs} = \frac{k_2k_3k_dk_a}{k_{-2}k_{-3}}$

The rate law (Eq. 13) is in accordance with the observed experimental results, wherein the order is unity in [oxo acid], [acid] and [NBS]. It is pertinent to mention here that the oxidation did not occur without the presence of mineral acid, and proceeded smoothly in the presence of added $[H_2SO_4]$ or $[HClO_4]$. The rate law (Eq. 13) can be rearranged to Eq. (14) which can be used for further verification.

$$\frac{1}{k} = \left[\frac{[\text{succinimide}]}{k_{obs}\,[\text{Oxo acid}][\mathrm{NBS}][\mathrm{H_3O^+}]}\right] \qquad (14)$$

According to Eq. (14) other conditions being constant, the plot of 1/*k* versus 1/[oxo acid] (Fig. 1) should be linear passing through the origin. Such an observation supports the validity of the rate law. (Eq. 14) and hence proposed reaction mechanism (Scheme 1). The proposed mechanism is further supported by the solvent influence on the reaction rate. The intermediate complex is less polar than the reactants due to dispersal of charge and hence, decreasing polarity of the solvent media is expected to stabilize the carbocationic reaction center in preference to reactants thereby enhancing the reaction rate. Such a solvent influence has actually been observed (Table 1).

Isokinetic relationship: The order of reactivity among the studied 5-oxo acids is: 4-methoxy > 4-methyl > -H > 4-chloro > 3-nitro phenyl substituted 5-oxo acids. The Hammett plots of log k versus σ (substituent constant) are linear, at all the studied temperatures. The reaction constant (**ρ**) is negative and decreases (in magnitude) with increasing temperature. The Hammett lines intersect at a point corresponding to a $\boldsymbol{\sigma}_{iso}$ value of –0.79 and a $\boldsymbol{k}_{iso}$ value of 63.09 x 10^{-3} s^{-1} **(**Fig. 5). An oxo acid with a substituent having this σ value (–0.79) will be oxidized by NBS with the same velocity at all temperatures. Such an insensitivity of the reaction rate to temperature is an indication for the existence of an isokinetic phenomenon. A reaction series that exhibits a common point of intersection in the Hammett plot is expected to have a common point of intersection in the Arrhenius plot (Fig. 3) also [28]. From the plots of $\Delta H^{\neq}$ against $\Delta S^{\neq}$, and ρ against 1/ T (Fig. 6), the T_{iso} value is found to be 357.14 K, which is in good agreement with the value (354.52) obtained from the slope of the Exner's plot (Fig. 4b). The isokinetic relationship in the present study implies that all the 5-oxo acids undergo oxidation by the same mechanism [29–32]. The isokinetic temperature ($\mathbf{T_{iso}}$) calculated as 357.14 K is higher than the highest temperature studied, indicating that the reaction rate is governed by the enthalpy of activation.



Scheme 1 Reaction Mechanism

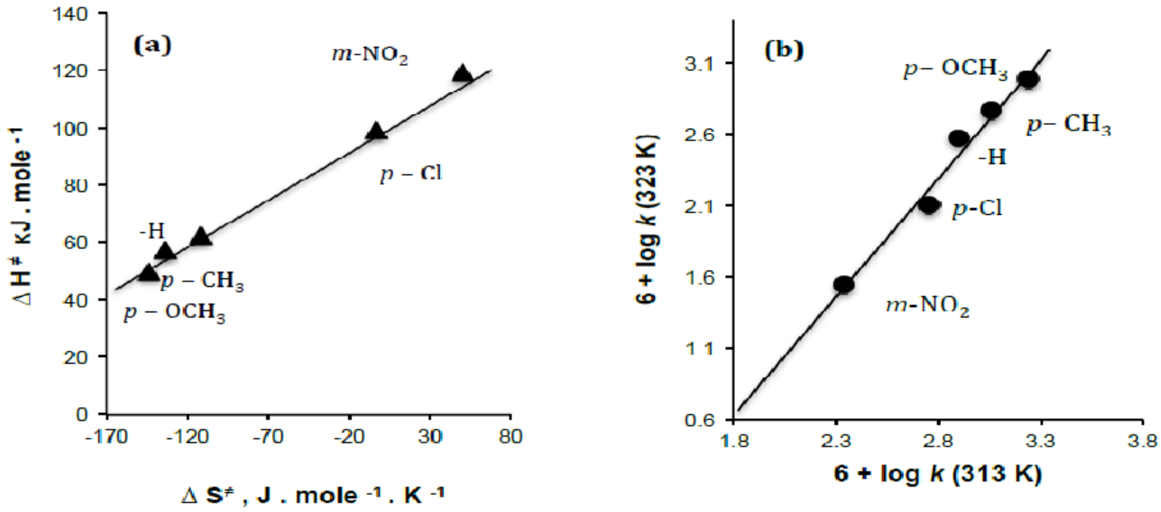


Fig 4: (a) Plot of $\Delta H^{\neq}$ versus $\Delta S^{\neq}$ and **(b)** Exner' s plot of log k (323 K) versus log k (313 K), showing the isokinetic relationship for the N-bromosuccinimide oxidation of 5-oxo acids.

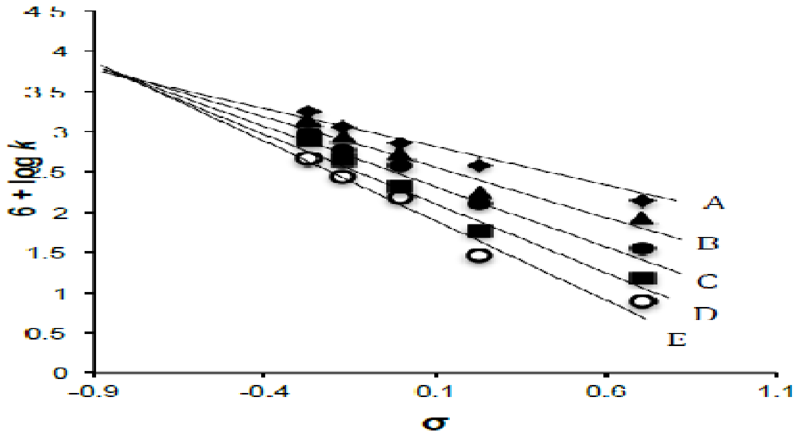


Fig 5: Hammett plots of log k against substituent constant (σ) at different temperatures showing the $\boldsymbol{k}_{iso}$ (s^{-1}) and $\boldsymbol{\sigma}_{iso}$ for the N-bromosuccinimide oxidation of 5-oxo acids.323 K , B) 318 K , C) 313 K, D) 308 K , E) 303 K.

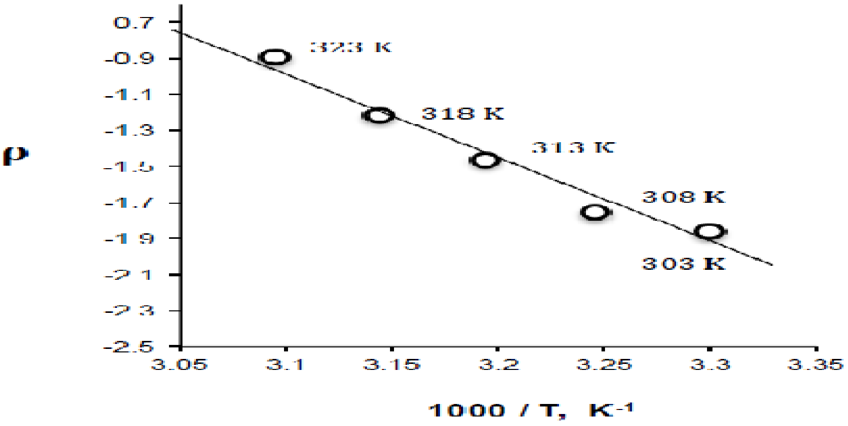


Fig 6: Plot of log $\boldsymbol{\rho}$ against 1/T for the N-bromosuccinimide oxidation of 5-oxo acids.

APPLICATIONS

The results suggest that this reaction could find utility as a selective route for the synthesis of benzoic acids. Indeed, this reaction is an example for the neighboring group participation with intramolecular catalysis in the oxidation of 5-oxo acids.

CONCLUSIONS

The oxygenation of 5-oxo acids with N-bromosuccinimide has been studied in aqueous acetic acid medium containing H_2SO_4. 5-oxo acids are converted into corresponding benzoic acids. Electron-releasing substituents accelerate the rate of oxidation and electron-withdrawing groups decelerate the rate. From the Hammett plot it is noted that the ρ value is negative and decrease with increase in temperature. The structure-activity correlations are made on the basis of results obtained and suggest positively charged reaction centre in the transition state. A mechanism involving the attack of active species of N-bromosucccinimide (H_2O^+Br) species on the enol-form of 5-oxo acids resulting in the cleavage of the carbon–carbon bond, yielding carboxylic acids has been proposed. The experimental protocol suggests that this reaction could find utility as a selective route for the synthesis of benzoic acids. Indeed, this reaction is an example for the neighboring group participation with intramolecular catalysis in the oxidation of 5-oxo acids.

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