Kinetics and mechanism of acid bromate oxidation of substituted 4-oxo acids

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Kinetics and mechanism of oxidation of substituted 4-oxo-4-arylbutanoic acids (4-oxo acids) by acid bromate (uncontaminated with Br_2) in aqueous acetic acid medium has been studied. The reaction exhibits first order each in [bromate] and [4-oxo acid] and second order in [acid]. Variation in ionic strength has no effect on the reaction rate, while the reaction rates are enhanced on lowering the dielectric constant of the reaction medium. Changing the solvent from H_2O to D_2O increases the rate of oxidation (k_{D_2O}/k_{H_2O} ~1.8). Electron releasing substituents in the aromatic ring accelerate the reaction rate and electron withdrawing substituents retard it. The order of reactivity among the studied 4-oxo acids is: *p*-methoxy>> *p*-methyl>-H> *p*-chloro> *m*-nitro. The Hammett's plot of log *k* versus σ is a smooth curve and concaves downward. However, the plot of log *k* against exalted sigma (Brown's σ^+) values is found to be linear with a slope of –1.50 at 313 K. The reaction constant (ρ^+) decreases with increase in temperature. The mechanism proposed involves the attack of the protonated bromate ($H_2Br^+O_3$) on the enol form of the 4-oxo acid giving the carbocationic bromate ester in the slow step, which undergoes cyclization and then on carbon-carbon bond cleavage yields the products in the fast step. From the intersection of lines in the Hammett and Arrhenius plots, the isokinetic relationship is discussed.

Among the various organic compounds employed in oxidative studies, 4-oxo acids are attractive substrates in terms of their enolization. These compounds readily undergo oxidation with various oxidants, unlike their corresponding carboxylic acids, and various mechanisms have been proposed. Formation of a complex between the oxidant and the enolic form of the 4-oxo acid in the slow step followed by its decomposition into products in the fast step, has been proposed in the oxidation by acid permanganate[1], N-chlorosuccinimide[2], N-bromosuccinimide[3], N-chloro-saccharin[4] and pyridinium fluorochromate[5]. Formation of an intermediate ester between the protonated 4-oxo acid and MnO_4^- in the equilibrium step followed by its breakdown to give products in the rate determining step has been proposed in the oxidation by permanganate in buffer media[6]. In the Os(VIII)-catalyzed oxidation by alkaline hexacyanoferrate(III) in sodium carbonate-bicarbonate buffer[7], the proposed mechanism involves complex formation between two similarly charged species, namely, the enolate anion of 4-oxo acid and $[OsO_4(OH)_2]^{2-}$ in the fast step, which decomposes into products in the slow step. In the alkaline hexacyanoferrate(III) oxidation of 4-oxo acids, a mesomeric radical-mediated mechanism, involving the

formation of enolate anion from the oxo compound and subsequent rate-determining electron transfer by the oxidant has been proposed by Rangappa *et al*[8].

Although acid bromate is a powerful oxidizing agent with a redox potential of 1.44 V, information on its use as an oxidant in the 4-oxo acid oxidation is lacking. Hence, to understand the type of mechanism and the products formed, the acid bromate oxidation of substituted oxo-acids was studies. This is of importance to exploit bromate for the oxidation of organic substrates, especially enolizable substrates like 4-oxo acids. The main objectives of the present study are to ascertain the reactive species of the substrate and oxidant, elucidate a plausible mechanism, deduce an appropriate rate law, identify the oxidation products, and, evaluate the kinetic and thermodynamic parameters.

Materials and Methods

KBrO$_3$ (Riedel) and mercuric acetate (Merck) were of analytical reagent grade and used as received. Acetic acid (BDH) was refluxed over chromic acid for 6 h and then distilled. D_2O (purity 99.4%) was obtained from BARC, Mumbai, India. The 4-oxo acids, 4-oxo-4-(4'-methoxyphenyl)butanoic acid, 4-oxo-4-(4'-methylphenyl)butanoic acid and

4-oxo-4-(4'-chloro phenyl)butanoic acid were obtained from Aldrich Chemical Co. 4-Oxo-4-(3'-nitro phenyl)butanoic acid was prepared from nitrobenzene and succinic anhydride in 1:1 mole ratio using anhydrous aluminium chloride as a catalyst[9]. All the 4-oxo acids were crystallized twice from water and their purity was checked by their melting points and UV, IR and NMR spectra. Solutions of the reagents were prepared either in doubly distilled water or in purified acetic acid and were standardized by the known methods. Fresh solutions were used for each kinetic run. Black coated Jena glass vessels were used to prevent photochemical effects, if any.

All absorption measurements were made with Shimadzu UV-visible spectrophotometer (MPS-5000) equipped with a temperature controller. Regression analyses of experimental data yielded the regression coefficient (r) and standard deviation (s).

Kinetic studies

The reaction mixture, containing 4-oxo acid, sulphuric acid and mercuric acetate solutions, was thermally equilibrated for an hour at the desired temperature under subdued light. The reaction was initiated by the addition of temperature-equilibrated bromate solution of requisite concentration. The rate of the reaction was followed by estimating the unreacted bromate iodometrically. All the reactions were carried out under the condition of using ten (or more)-fold excess of [4-oxo acid] over [bromate]. The pseudo-first order rate constants (s^{-1}) were computed from linear plots of log [bromate]$_t$ against time ($r \geq 0.98$; $s \leq 0.03$) up to 90% completion of the reaction, the rate constants (k) were reproducible within 5%. Rate constants did not alter in nitrogen atmosphere and all the rate constants reported in this paper were obtained without nitrogen. Freshly prepared solutions of oxo acids in purified acetic acid were used to avoid any possible side reactions.

The stoichiometry of the reaction was determined by equilibrating reaction mixture of various [bromate] /[4-oxo acid] ratios at 40° C for 12 h, keeping all other reagents constant. Estimation of unconsumed bromate (iodometrically) revealed that one mole of 4-oxo acid consumed one mole of bromate (Eq. 1).

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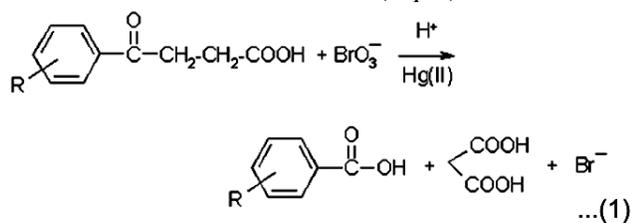
The products were extracted with ether, dried and analyzed. Benzoic acid was identified by its m.pt. (121 °C) and estimated quantitatively with a standard curve at λ_{max} = 235 nm. Malonic acid was identified by its m.pt. (135 °C) and also tested with its characteristic spot test through conversion into barbituric acid[10]. Identification of the products, namely, benzoic and malonic acids, were also made by comparing the R_f values of the authentic samples. Bromide ion was identified by adding AgNO$_3$ solution, resulting in the formation of pale yellow AgBr precipitate.

Results and Discussion

The reduction of bromate with excess [4-oxo acid] is auto-catalytic. The oxo acid reacts with bromate forming Br$_2$ and HOBr, which are further reduced to Br$^-$ ions. The kinetics of the reaction of oxo acid with Br$_2$ has been studied and it was found that $k_{HOBr} > k_{Br_2}$. Tribromide ions are kinetically inactive, hence, bromate ions are consumed not only by the reaction with oxo acid but also by the reaction with Br$^-$ ions. If bromide ions are masked in the solution by adding a suitable complexing agent such as mercury(II), the Br$^-$ ions cannot take part in follow up reactions and the overall reaction loses its auto-catalytic character. This is exactly what was observed with the addition of mercury(II) acetate. The added Hg(II) ions formed non-ionized mercury(II)-bromocomplexes of high stability constants[11,12] (HgBr$^+$, K_1 = 2.51 × 10^8 dm^3 mol^{-1}; HgBr$_2$, K_2 = 3.8 × 10^8 dm^3 mol^{-1}) and the kinetic results remained the same over a wide concentration range (0.001-0.01 mol dm^{-3}) of mercuric acetate. Control experiments, performed in the absence of the substrate, did not show any appreciable change in [bromate]. In order to mask the Br$^-$ ions formed, an optimum concentration of mercuric acetate (0.005 mol dm^{-3}) was employed. Therefore, the reported rate constants and thermodynamic parameters pertain to pure bromate (uncontaminated with Br$_2$) oxidation only.

At fixed concentrations of acid, mercuric acetate and ten-fold excess of [substrate], the decrease in [bromate] followed first order kinetics. The first order rate constants, (k_1) were calculated from the linear plots ($r \geq 0.98$, $s \leq 0.03$) of log [bromate]$_t$ against time. Such plots are linear for more than three half-lives of the reaction (Fig. 1). The k_1 value was independent of initial [bromate] for all the studied substrates.

The reactions for all the studied 4-oxo acids are first order in the [substrate] (Table 1), and in $[H^+]^2$ in the range of 0.5 – 4.0 mol dm^{-3} sulphuric acid (Table 2). From the Zucker-Hammett plots of log k versus $-H_0$, the slopes obtained were in the range of 1.0–1.2, indicating the non-involvement of water molecule in the rate determining step. The H_0 values were taken from Paul and Long[13] assuming that the H_0 values do not change much in a media containing acetic acid up to 50%.

The effect of dielectric constant (D) on the rate of reaction was studied by varying acetic acid–water content in the reaction mixture. Acetic acid does not react with the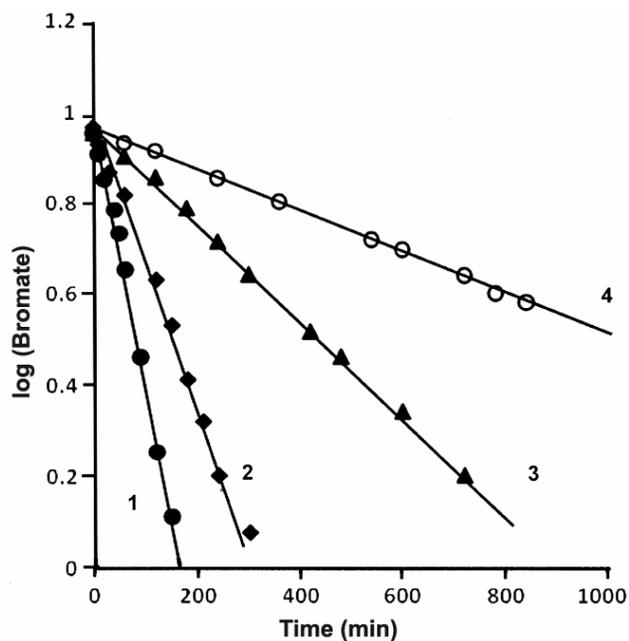 oxidants[14], yet rate of the reaction is enhanced by increasing acetic acid content of the medium (Table 3). Also, log k against $1/D$ is found linear, suggesting a positive ion-dipole type of interaction[15] in the rate determining step.

There was no induced polymerization of acrylonitrile monomer, ruling out the possibility of free radical formation during the course of the reaction.

Rate of oxidation increased in the D_2O medium ($k_{D2O}/k_{H2O} \sim 1.8$). Since D_3O^+ is about three times stronger acid than H_3O^+ (refs 16, 17), the solvent isotope effect suggests a proton-catalyzed reaction.

In the temperature range of 298 – 323 K in 2.0 mol dm^{-3} sulphuric acid and acetic acid–water

Fig. 1 — Typical first order plots in the acid bromate oxidation of 4-oxo acids. [1, p–CH₃; 2, –H; 3, p–Cl; 4, m–NO₂].

Table 1 — Effect of varying [substrate] on the rate of acid bromate oxidation of 4-oxo acids at 313 $\pm$ 0.1 K. {[Bromate] = 0.001 mol dm^{-3}; [H₂SO₄] = 2.0 mol dm^{-3}; [Hg (OAc)₂] = 0.005 mol dm^{-3}; HOAc – H₂O = 1 : 1 % (v/v)}

[4-oxo acid] (mol dm^{-3})	$10^5 \times k_{obs}$ (s^{-1})[a]				
	-H	p-OCH₃	p-CH₃	p-Cl	m-NO₂
0.005	6.35	95.9	13.43	2.13	0.7 6
0.01	12.79	191.9	26.86	4.26	1.51
0.015	19.19	287.8	40.32	6.39	2.33
0.02	25.58	383.8	53.72	8.52	3.04
0.03	38.13	575.7	80.59	12.79	4.55
0.04	51.12	767.6	107.4	17.14	6.04
0.06	76.74	1151	161.2	25.58	9.11

[a]Mean of duplicate experiments

Table 2 — Effect of varying [H₂SO₄] on the rate of acid bromate oxidation of 4-oxo acids at 313 $\pm$ 0.1 K. {[Substrate] = 0.01 mol dm^{-3}; [bromate] = 0.001 mol dm^{-3}; [Hg (OAc)₂] = 0.005 mol dm^{-3}; HOAc – H₂O = 1 : 1 % (v/v)}.

[H₂SO₄] (mol dm^{-3})	$-H_0$	$10^5 \times k$ (s^{-1})[a]				
		-H	p-OCH₃	p-CH₃	p-Cl	m-NO₂
0.5	-0.13	1.59	11.88	2.30	-	-
0.75	0.07	2.87	29.92	4.39	-	-
1.00	0.26	4.51	47.97	7.67	1.27	1.19
1.50	0.56	8.83	95.95	15.99	2.32	1.25
2.00	0.84	12.79	191.9	26.86	4.26	1.51
2.50	1.12	25.58	287.8	47.97	7.19	2.55
3.00	1.38	34.84	479.7	134.3	12.79	3.99
4.00	1.85	57.57	1151	287.8	25.58	7.67
s[b]		2.00	2.0	2.0	2.01	2.00
n[c]		1.0	1.2	1.0	1.1	1.0

[a]Mean of duplicate experiments;
[b] Slopes of log k versus log [H₂SO₄];
[c]Slopes of Zucker-Hammett plots.

Table 3 — Effect of varying solvent composition on the rate of acid bromate oxidation of 4-oxo acids at 313 $\pm$ 0.1 K. {[Substrate] = 0.01 mol dm^{-3}; [bromate] = 0.001 mol dm^{-3}; [H₂SO₄] = 2.0 mol dm^{-3};[Hg (OAc)₂] = 0.005 mol dm^{-3}}

ACOH – H₂O (v/v, %)	$10^5 \times k$ (s^{-1})[b]				
	-H	p- OCH₃	p-CH₃	p-Cl	m-NO₂
30-70 (53.18)	7.59	63.9	9.49	2.39	1.17
40-60 (46.48)	9.59	115.1	13.09	3.09	1.27
50-50 (39.78)	12.79	191.9	26.86	4.26	1.51
60-40 (33.08)	15.89	586	44.69	7.19	1.74
70-30 (26.38)	38.29	1751	162.9	12.79	2.68

[a]Values of dielectric constant of the media are given in parentheses;
[b]Mean of duplicate experiments.

medium (50% v/v) (Fig. 2) the activation energy (E_a) and related thermodynamic parameters ($\Delta H^{\ddagger}$, $\Delta G^{\ddagger}$ and $\Delta S^{\ddagger}$) were evaluated. The plot between $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ is linear (Fig. 3, $r \geq 0.98$, $s \leq 0.028$) and the isokinetic temperature (ß) obtained is 357 K. The isokinetic relationship in the present study implies that all the 4-oxo acids undergo oxidation by the same mechanism[18].

The effect of substituents on the rate of oxidation was studied using different phenyl substituted 4-oxo acids (ArCOCH$_2$CH$_2$COOH, where Ar = 4-methoxy, 4-methyl, 4-chloro and 3-nitro substituted phenyl) at different temperatures. In all these cases, the reaction orders are the same, namely, first order with respect to [oxidant] and [substrate], and second order with respect to [acid]. Electron releasing substituents in the phenyl ring enhance the rate of oxidation and electron withdrawing substituents decrease it (Table 4). The order of reactivity among the studied 4-oxo acids is: 4-methoxy>>4-methyl>-H>4-chloro>3-nitro phenyl substituted 4-oxo acids. The Hammett plots of log k versus σ (substituent constant) are smooth curves and concave downward, at all the studied temperatures. However, the Hammett plots are linear with good correlation coefficient at four different temperatures when exalted substituent constant (Brown's σ$^+$) values

are used (Fig. 4). The reaction constant (ρ$^+$) is negative and decreases (in magnitude) from -1.66 to -1.33 with increasing temperature from 303 K to 323 K The Hammett lines intersect at a point corresponding to a σ$^+_{iso}$ value of -1.42 and a k_{iso} value of 13.18 × 10^{-3} s^{-1} (Fig. 4). An oxo acid with a substituent having this σ$^+$ value (-1.42) will be oxidized by acid bromate with the same rate at all temperatures. Such an insensitivity of the reaction rate to temperature is a pointer to the existence of an isokinetic phenomenon.

Table 4 — Effect of substituent on the rate of oxidation of 4-oxo acids by acid bromate at 313 ± 0.1 K. {[Substrate] = 0.01 mol dm^{-3}; [bromate] = 0.001 mol dm^{-3}; [H$_2$SO$_4$] = 2.0 mol dm^{-3}; [Hg (OAc)$_2$] = 0.005 mol dm^{-3}; HOAc – H$_2$O = 1 : 1 % v/v}.

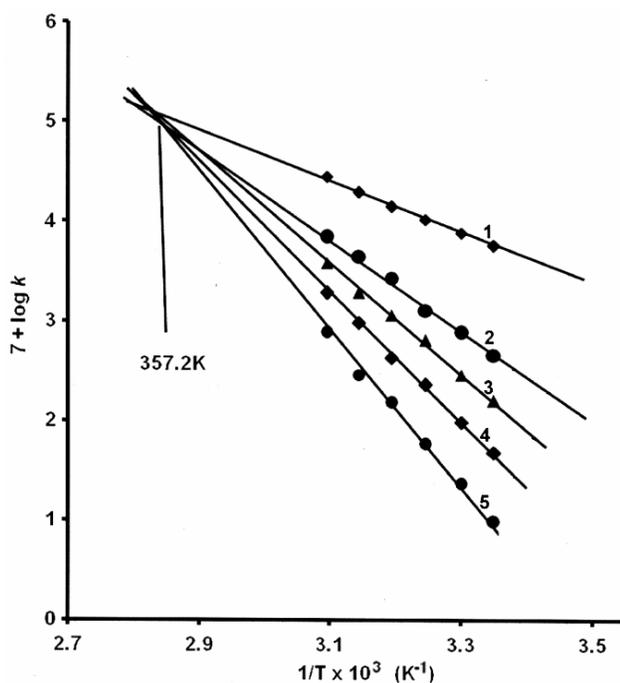| Substituent	σ	σ$^+$	$10^5 \times k$ (s^{-1})	5 + log k
-H	0.00	0.00	12.8	1.1070
p-OCH$_3$	-0.27	-0.78	191.9	2.2830
p-CH$_3$	-0.17	-0.31	26.9	1.4292
p-Cl	0.23	0.11	4.3	0.6298
m-NO$_2$	0.71	0.67	1.5	0.1802

Fig. 2 — Arrhenius plots of log k against $1/T$ showing the isokinetic temperature. [1, p–OCH$_3$; 2, p–CH$_3$; 3, –H; 4, p–Cl; 5, m–NO$_2$].
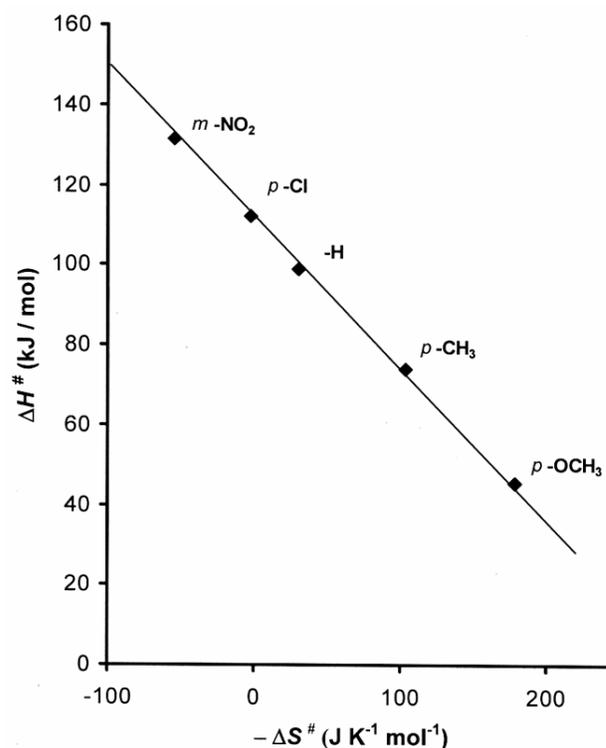

Fig. 3 — Plot of $\Delta H^{\#}$ against $-\Delta S^{\#}$ showing the isokinetic relationship.
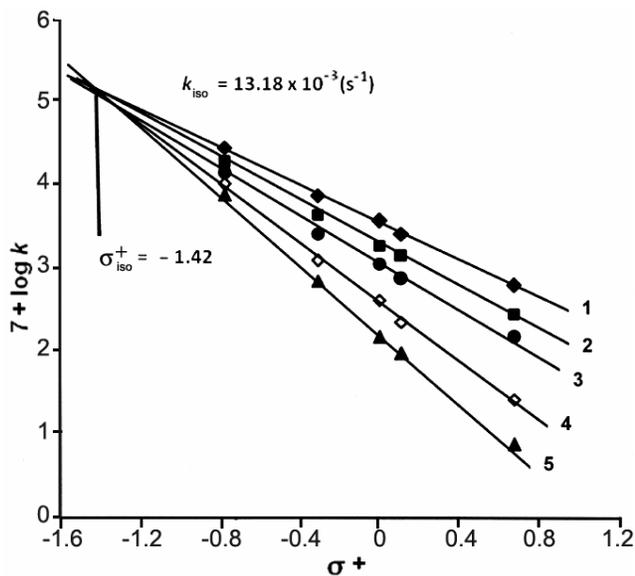
Fig. 4 — Hammett plots of log k against σ^+ at different temperatures. [1, 323 K; 2, 318 K; 3, 313 K; 4, 308 K, 5, 303 K].

A reaction series which exhibit a common point of intersection in the Hammett plot (Fig. 4) is expected to have a common point of intersection in the Arrhenius plot also[33] (Fig. 2). From the plots of $\Delta H^{\ddagger}$ against $\Delta S^{\ddagger}$, and ρ against $1/T$, the T_{iso} value is found to be 357 K, which is in good agreement with the value obtained from the slope of the Exner's plot.

In acid solutions, the reactive species of bromate are likely to be BrO_3^- and protonated bromate ($HBrO_3$ or $H_2Br^+O_3/Br^+O_2$). Hence, the oxidation may be a reaction involving one of the oxidant species. The effect of solvent polarity and the acceleration in the rate with increase in [acid] mitigate the possibility of unprotonated bromate (BrO_3^-) to be the reactive species. Amis et al.[19] proposed Br^+O_2 as one such oxidizing species. Anbar and Guttmann[20], as well Wright and Barton[21] suggested that, in moderately strong acid solutions, $H_2X^+O_3$ is the existing form of halate ion and in the case of bromate $H_2Br^+O_3$, Beck et al.[22] and Reddy and Sundaram[23] also suggested $H_2Br^+O_3$ as the active species of bromate in moderately strong acid solutions, with a protonation constant of 0.21 $dm^6\ mol^{-2}$.

The enhancement of reaction rate with an increase in the amount of acetic acid and linear plots of log k versus $1/D$ with positive slopes indicate an interaction between a positive ion and a dipole molecule in the slow step. This supports the postulation of $H_2Br^+O_3$ as the reactive species of bromate in the acid medium.

The rate acceleration with an increase in [acid] and second order dependence of rate on [acid] in the range studied also confirm that $H_2Br^+O_3$ is the reactive species of bromate taking part in the oxidation of 4-oxo acids.

The 4-oxo acid is a weak acid (pK_a = 5.77 at 40 ^oC in aqueous solution, ref. 6) and the undissociated form of the substrate can be taken as the only form in acidic media.

In acid solutions, 4-oxo acid undergoes keto enol tautomerism (Eq. 2).
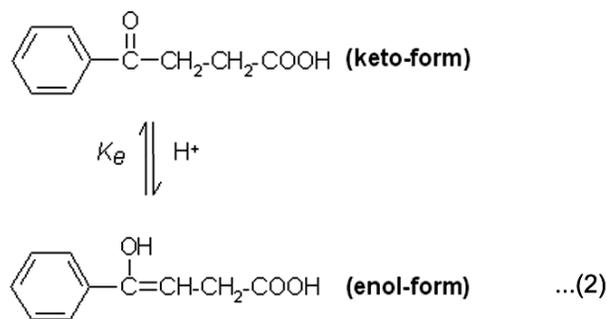
In oxidation reactions, the keto group of the substrate can react either directly, or through the enol form. Oxidation rates faster than the rates of enolization have been observed with ceric ion[24], manganic ion[25], cobaltic and vanadate ions[26], mercuric perchlorate[27] and alkaline diperiodate argentate(III) (ref. 28) as oxidants, indicating that the keto group of the substrate reacts directly. All of these oxidants undergo one-electron reduction, and the reactions proceeded via a free radical mechanism[24–28].

The rates of oxidation and enolization were found to be equal in the oxidation reactions by manganic pyrophosphate[29], thallium triacetate[30] and by diperiodatonickelate(IV) (ref. 31). These reactions were zero order in [oxidant], indicating the enol formation as the rate determining step.

In the present investigation, the rate of enolization (measured by the bromination method[32]) is greater than the rate of oxidation by a factor of ~ 13–15 and the enolization step can be visualized as proceeding via the enol form of the keto group of 4-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. The most plausible mechanism therefore seems to be as shown in Scheme 1.
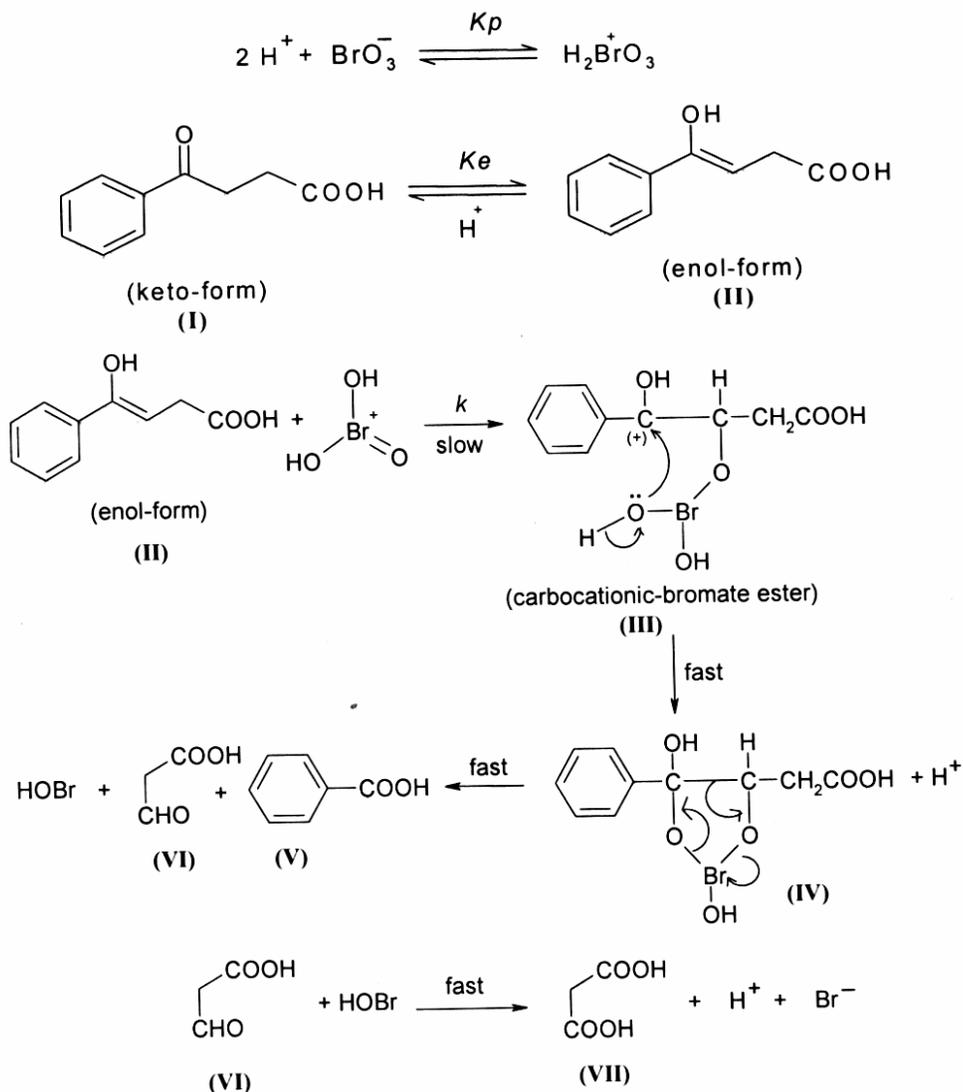
Scheme 1

Formation of formyl acetic acid as the intermediate was confirmed by comparing with the R_f value of the authentic sample. Benzoic and malonic acids were the final products of oxidation.

It is pertinent to point out here that malonic acid is stable and does not undergo further oxidation with bromate in acid medium[11]. The proposed mechanism is also in accordance with the observed stoichiometry. The rate equation in consonance with the mechanism proposed is as given in Eq. (3).

$$\frac{-d[\text{BrO}_3^-]}{dt} = K_p K_e k [\text{H}^+]^2 [4-\text{oxoacid}][\text{BrO}_3^-]$$

...(3)

The obtained rate law could explain the second order in [acid] and first order each in [bromate] and [4-oxo acid].

Conclusions

The above study shows that the protonated bromate reacts with the enol form of 4-oxo acid in the rate determining step, giving the cyclic bromate ester. Decomposition of the bromate ester results in the cleavage of the carbon–carbon bond, yielding carboxylic acids. This experimental protocol suggests that this reaction could find utility as a regioselective route for the synthesis of carboxylic acids, specially malonic and benzoic acids.

Acknowledgement

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