

Kinetics & Mechanism of Oxidation of Hydroxyacids by Aqueous Bromine

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Received 24 August 1978; revised 14 April 1979; accepted 20 July 1979

Kinetics of oxidation of glycollic, lactic, α -hydroxyisobutyric, mandelic and *p*-chloro- and *p*-bromo-mandelic acids by aq. bromine at pH 3-5 have been investigated. The order of reaction in Br₂ and substrate is one each. The reaction rate is inversely proportional to [Br⁻]. Increase in pH increases the reaction rate. Neither primary hydrogen isotope effect (k_H/k_D) nor solvent isotope effect (k_{H_2O}/k_{D_2O}) has been observed in the reaction of mandelic acid with bromine. A suitable mechanism consistent with the data is suggested.

IN the oxidation of mandelic acid and related compounds Auckett and Barker¹ observed that the undissociated hydroxyacid and its anion react with bromine, the latter reacting 9.5 times faster than the former. The reaction with HOBr is about 12 times faster than that with bromine molecule. Pink and Stewart² have reported that at pH > 6, anion of the acid reacts with bromine as well as with HOBr. Recently, Rathore and Grover³ have suggested bromine and not HOBr as an active oxidant in the oxidation of lactic acid with bromine. Thus, the conclusions of various workers appeared conflicting. It was, therefore, considered necessary to reinvestigate the oxidation of α -hydroxyacids by Br₂ at pH 3-5 with a view to ascertaining (i) the active oxidising species; (ii) the relative rates of oxidation of anion and the undissociated form of hydroxyacids; and (iii) the effect of structure on the rate. The results of such a study are reported in the present paper.

Materials and Methods

Chemicals used were either pure or were purified by conventional methods. *p*-chloro⁴ and deuterated† (α -D)⁵ mandelic acids were prepared in the laboratory.

The reaction was carried out at constant pH using aq. acetate buffers (0.3M). The reaction vessels were blackened from outside to prevent the photochemical effect. Reactants were brought to thermostatic temperature ($\pm 0.02^\circ$) and the reaction was initiated by adding appropriate volume of substrate. The progress of reaction was monitored by estimating the unreacted Br₂ iodometrically.

At [Substrate] \gg [Br₂], acetone was found to be the oxidation product of α -hydroxyisobutyric acid; in all other cases (except malic acid for which products could not be confirmed) corresponding

aldehydes were detected as their 2, 4-dinitrophenyl hydrazones and finally characterised by m. m.p. determination.

Results and Discussion

The order of reaction is one each with respect to total bromine (Br₂ and Br₂⁻) (Table 1) hydroxyacid (Table 2). Addition of Br⁻ retards the rate of reaction (Table 3). In all the cases a plot of $1/k_1$ against [Br⁻] is linear. Assuming Br₂, Br₂⁻ and HOBr to be the active oxidising species, the rate constant k'_1 , in the presence of Br⁻, can be expressed as :

$$k'_1 = \frac{1}{K + [Br^-]} \left\{ k_1 K + k_2 [Br^-] + \frac{k_3 K K_h}{[H^+][Br^-]} \right\} \quad \dots (1)$$

Where K dissociation constant of the equilibrium

TABLE 1 — EFFECT OF VARYING INITIAL [Br₂] ON THE RATE OF OXIDATION OF GLYCOLLIC ACID

{[Glycollic acid] = $2.66 \times 10^{-3}M$; pH = 3.40; temp. = 29°}

[Bromine] $\times 10^3 M$	$k_1 \times 10^3$ min ⁻¹
1.66	5.90
3.33	6.00
5.00	6.00

TABLE 2 — EFFECT OF VARYING [GLYCOLLIC ACID] ON THE REACTION RATE

{[Bromine] = $3.33 \times 10^{-3}M$; pH = 3.40; temp. = 29°}

[Glycollic acid] $\times 10^3 M$	$k_1 \times 10^3$ min ⁻¹	$k_1/[Glycollic acid]$
2.00	4.60	2.30
2.66	6.00	2.26
3.00	7.00	2.33
3.33	7.76	2.34

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‡Extent of deuteration was estimated by PMR spectrum. The authors are thankful to Prof. B. Venkataraman and Dr Govil of TIFR, Bombay for PMR.

TABLE 3 — VALUES OF THE DISSOCIATION CONSTANT (K) OF THE TRIBROMIDE ION AT $[Br_2] = 3.33 \times 10^{-3} M$

$k \times 10^{-2} \text{ mole}^{-1} \text{ at } [Br^-]$	$[Br^-]$			pH	temp. (0°C)	K(calculated) moles litre ⁻¹			
	5×10^{-3}	10×10^{-3}	$15 \times 10^{-3} M$						
6.00	[Glycollic acid] = 3.66×10^{-3}			3.45	2.35	1.78	3.40	29.0	0.064
6.45	[Lactic acid] = $5.30 \times 10^{-3} M$			3.75	2.60	2.00	3.50	33.0	0.067
10.3	[α -Hydroxyisobutyric acid] = $2.0 \times 10^{-3} M$			5.65	3.84	2.92	3.25	28.3	0.059
5.10	[Malic acid] = $2.0 \times 10^{-3} M$			2.86	2.00	1.52	3.50	35.0	0.064
5.18	[Mandelic acid] = 2.66×10^{-3}			2.86	2.00	1.52	3.30	29.0	0.062

$Br_2 + Br^- \rightleftharpoons Br_3^-$ K_n is the hydrolysis constant for the reaction:



and k_1 , K_2 and k_3 are the rate constants corresponding to the reactions of Br_2 , Br_3^- and $HOBr$ with the substrate respectively.

The plot of k'_1 versus $\frac{1}{K + [Br^-]}$ is linear passing

through the origin. To evaluate $1/k + [Br^-]$, the value of k was taken to be 0.06. (ref. 6). The fact that the plot is linear rules out any significant contribution of the k_3 term. Then Eq. 1 reduces to:

$$k'_1 = \frac{1}{K + [Br^-]} \{ k_1 K + k_2 [Br^-] \} \quad \dots(2)$$

As $1/(K + [Br^-])$ approaches zero, concentration of Br^- should tend to infinity. Had there been a contribution of the second term to k'_1 the plot would not have passed through the origin but would have cut k'_1 axis corresponding to $k_2 [Br^-]$. Alternatively, $k'_1 \{K + [Br^-]\}$ comes out to be constant within experimental conditions. Hence the contribution of k_2 term to k'_1 is also ruled out. Br_2 is, therefore, the only reactive species under experimental conditions. Eq. (2) therefore reduces to:

$$k'_1 = \frac{k_1 K}{K + [Br^-]} \quad \dots(3)$$

and can be rearranged as

$$\frac{1}{k'_1} = \frac{1}{k_1} + \frac{[Br^-]}{K k_1} \quad \dots(4)$$

The plot of $1/k'_1$ versus $[Br^-]$ is linear with a slope $[Br^-]/k_1 K$ and intercept $1/k_1$. This gives a check on the values of k_1 obtained without adding initial $[Br^-]$ and also the values of dissociation constant of tribromide ion. The value of K (ranging from 0.062 to 0.064) (Table 3) thus obtained agree well with the value of 0.0594 mole litre⁻¹ reported by Scaife and Tyrell⁶. The fact that a plot of $\log(a-x)$ versus t is linear even in the presence of accumula-

ting Br^- ions needs an explanation. On rearranging the Eq. (3) we get

$$k'_1 = \frac{k_1}{1 + [Br^-]/K} \quad \dots(5)$$

If $[Br^-] K < 1$ then $k'_1 \cong k_1$. In case no Br^- ions are added the maximum $[Br^-] = 6.0 \times 10^{-3} M$ and hence $[Br^-]/K < 1$ making $k'_1 \cong k_1$.

The Reaction rate increases with the increase in pH in all the cases (Table 4 for a typical case). Since Br_2 is the only oxidising species within the pH range studied, the increase in rate with increase in pH can only be explained by assuming the anion of the hydroxy acid to react faster than the undissociated acid with Br_2 . If k_A^- and k_{HA} are the rate constants for the reaction of Br_2 with anion and undissociated acid respectively, then the second order rate constant (k_2) can be expressed as:

$$k_2 = \frac{k_1}{[\text{acid}]} = k_A \cdot \alpha + k_{HA} \cdot (1 - \alpha) \quad \dots(6)$$

where α is the mole fraction of the anion.

$$\text{Using } K_a = \frac{[H^+][A^-]}{[HA]} \text{ and } \alpha = \frac{[A^-]}{[HA]_T}$$

Eq. (6) becomes:

$$k_2 \{K_a + [H^+]\} = k_A^- \cdot K_a + k_{HA} [H^+] \quad \dots(7)$$

From the slope and intercept of a linear plot of $k_2 \{K_a + [H^+]\}$ versus $[H^+]$ (Fig. 1 for a typical case) the values of k_A^- and k_{HA} were calculated (Table

 TABLE 4 — EFFECT OF HYDROGEN IONS ON REACTION RATE OF GLYCOLLIC ACID
 {(Glycollic acid) = $2.66 \times 10^{-2} M$; $[Br_2] = 3.33 \times 10^{-3} M$
 temp. = 29°}

pH	$[H^+] \times 10^7$ M	$k_1 \times 10^3$ min ⁻¹	$10^5 \cdot k_2 \{k_a + [H^+]\}$ [Glycollic acid]
3.40	3.98	5.90	12.10
3.70	2.00	6.25	8.18
4.0	1.00	6.90	6(43)
5.0	0.10	7.83	6.45

$$K_a = 1.48 \times 10^{-4}; pK = 3.83;$$

$$k_A = 0.30 \text{ litre mole}^{-1} \text{ min}^{-1}; k_{HA} = 0.19 \text{ litre mole}^{-1} \text{ min}^{-1}$$

 TABLE 5 — VALUES OF k , k_A AND k_{HA} AT 35° FOR DIFFERENT SUBSTRATES

Substrate	p k_a	$k \times 10^3$ (litre mole ⁻¹ sec ⁻¹)	$k_A \times 10^3$ (litre mole ⁻¹ sec ⁻¹)	$k_{HA} \times 10^3$ (litre mole ⁻¹ sec ⁻¹)	Ratio k_A/k_{HA}
Glycollic acid	3.83	5.26	7.00	4.61	1.52
Lactic acid	3.87	23.5	31.6	20.2	1.56
α -Hydroxyisobutyric acid	4.17	15.3	24.0	12.2	1.97
Mallic acid	3.46	3.77	5.76	1.71	3.37
Mandelic acid	3.45	55.7	79.6	28.5	2.80
p-Bromomandelic acid	3.30	43.8	55.0	26.6	2.07
p-Chloromandelic acid	3.30	44.7	56.6	26.3	2.15

TABLE 6 — EFFECT OF TEMPERATURE ON THE RATE OF REACTION

$$\{[\text{Substrate}] = 2.66 \times 10^{-2}M, \text{pH } 3.50; [\text{Br}_2] = 3.3310^{-3}M\}$$

Substrate	$k_a \times 10^3$ (mole litre ⁻¹ sec ⁻¹) at temp. (°C)					ΔE^\ddagger (k cal mole ⁻¹)	ΔS^\ddagger (e.u.)
	298	303	308	313	318		
Glycollic acid	0.29	0.37	0.52	0.73	—	11.9	—31.0
Malic acid	—	0.26	0.37	0.55	0.79	14.6	—22.9
Lactic acid	1.10	1.55	2.01	3.00	4.25	14.1	—20.7
α -Hydroxy-isobutyric acid*	0.85	1.13	1.50	2.16	—	13.9	—22.6
	(301.3)	(305.2)	(309.0)	(314)			
Mandelic acid	—	3.68	5.56	7.88	11.01	13.4	—19.6
<i>p</i> -Bromomandelic acid†	—	2.98	4.40	6.43	9.00	14.2	—19.4
<i>p</i> -Chloromandelic acid*	—	3.03	4.46	6.50	9.21	14.3	—18.9

*Values at pH = 3.25; †[Substrate] = $5.33 \times 10^{-2}M$

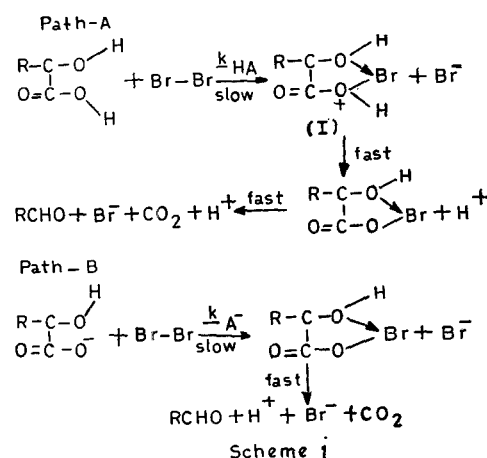
5). The results show that anion reacts 1.3-3.5 times faster than the acid with Br_2 . This is much lower than the value (≈ 9.5) obtained by Auckett and Barker¹ for mandelic acid and is very much less than that obtained for glucose and its anion⁷ ($\approx 10^{10}$). The high reaction rate in case of glucose is explained on the basis of difference in energies of activation of the reaction of glucose ($18.3 \text{ k cal/mole}^{-1}$) and its anion ($5.01 \text{ k cal mole}^{-1}$) with Br_2 . Since the value of $k_{\text{A}^-} / k_{\text{HA}}$ is small in the present case, the above explanation for the higher value of k_{A^-} is not valid. It appears that ΔE^\ddagger for the reaction of acid and its anion with Br_2 is practically the same and that the difference in the value of k_{A^-} and k_{HA} can be interpreted in terms of small difference in the ΔS^\ddagger values of these reactions.

The reactions were studied at different temperatures, and activation parameters calculated (Table 6). The negative entropy of activation suggests that the activated complex is highly polarised as compared to reactant molecules, and/or a cyclic intermediate is formed in the rate limiting step.

Neither primary kinetic hydrogen isotope effect $k(\alpha\text{-H}) / k(\alpha\text{-D})$ nor solvent isotope effect $k_{\text{H}_2\text{O}} / k_{\text{D}_2\text{O}}$ was observed in the reaction of mandelic acid with Br_2 .

The mechanism of reaction as shown in Scheme 1 by Path A and B is in accord with the experimental observations.

The rate of formation of hypobromite intermediate (I and II) will certainly be faster for anion (II) than the undissociated hydroxyacid (I). This is also in accord with the data given in Table 5 where the order in which pK_a of the acids vary is identical to that in which the rates of oxidation vary. The fact that formation (I) / (II) is anchimerically assis-



ted by the neighbouring oxygen atom precludes any correlation with σ , the substituent constants (Taft-plot).

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