Kinetics and mechanism of the oxidation of α-hydroxy acids by benzyltrimethylammonium chlorobromate

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Abstract. The oxidation of glycollic, lactic, malic and a few substituted mandelic acids by benzyltrimethylammonium chlorobromate (BTMACB) in acetic acid–water (1:1) leads to the formation of the corresponding oxoacids. The reaction is of first order in BTMACB as well as the hydroxy acid. Addition of benzyltrimethylammonium chloride or bromide ion does not affect the rate indicating that BTMACB itself is the reactive oxidizing species. The oxidation of α-deuteriomandelic acid shows the presence of a primary kinetic isotope effect ($k_H/k_D = 5.27$ at 303 K). The reaction does not exhibit the solvent isotope effect [$k(H_2O)/k(D_2O) = 1.01$]. The rate decreases with increase in the amount of acetic acid in the solvent mixture. A mechanism is proposed which involves hydride ion transfer to the oxidant.

Keywords. α-Hydroxy acids; benzyltrimethylammonium chlorobromate; kinetic isotope effect; hydride ion transfer.

1. Introduction

Benzyltrimethylammonium polyhalides are widely used as halogenating reagents in synthetic organic chemistry[1,2]. Recently, polymeric benzyltriethylammonium dichloro-iodate and dibromoiodate have been used for the halogen addition reactions of olefins[3]. There are, however, only a few reports regarding their use as oxidizing agents in synthetic chemistry[4–6]. These compounds are more suitable for oxidation than molecular halogens because of their solid nature, ease of handling, stability, selectivity and excellent product yields. We have been interested in the kinetic and mechanistic studies of the reactions of polyhalides and many reports have already emanated from our laboratory[7–10]. Hydroxyacids can be oxidised either like alcohols[11] or they may undergo oxidative decarboxylation[12]. There seems to be no report on the oxidation of α-hydroxyacids by benzyltrimethylammonium chlorobromate (BTMACB). In this article we report the kinetics of oxidation of glycollic acid (GA), lactic acid (LA), malic acid (MLA) and monosubstituted mandelic acids (MA) by BTMACB, in aqueous acetic acid.

2. Experimental

2.1 Materials

All the hydroxy acids used were commercial products of the highest purity available and were used as such. BTMACB was prepared by the reported method[1] and its purity

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checked by the iodometric method. α-Deuteriomandelic acid (PhCD(OH)COOH or DMA) was prepared by the method of Kemp and Waters [13]. Its isotopic purity, ascertained by NMR spectra, was $93 \pm 4\%$. Acetic acid was purified by refluxing with chromic oxide and acetic anhydride for 6 h and then fractional distillation [14].

2.2 *Product analysis*

Product analysis was carried out under kinetic conditions, i.e. with an excess of the reductant over BTMACB. In a typical experiment, mandelic acid (7.6 g, 0.05 mol) and BTMACB (3.46 g, 0.01 mol) were dissolved in 100 ml of 1:1 (v/v) acetic acid–water and allowed to stand in the dark for $\approx$ 24 h to ensure the completion of the reaction. The mixture was then treated overnight with an excess (250 ml) of a freshly prepared saturated solution of 2,4-dinitrophenylhydrazine in 2 mol l^{-1} HCl. The precipitated 2,4-dinitrophenylhydrazone (DNP) was filtered off, dried, weighed, recrystallized from ethanol and weighed again. The product was identical (m.p. and mixed m.p.) to an authentic sample of DNP of phenylglyoxalic acid. The yields of the DNP, before and after recrystallization, were 2.27 g (93%) and 2.01 g (82%) respectively. Similar experiments with other hydroxy acids yielded the DNP of the corresponding oxoacids in 78–89% yields after recrystallization.

2.3 *Kinetic measurements*

Pseudo-first-order conditions were attained by maintaining an excess ($\times$ 15 or greater) of the [hydroxy acid] over [BTMACB]. The solvent was 1:1 (v/v) acetic acid–water. The reactions were studied at constant temperature ($\pm$ 0.1 K) and were followed by monitoring the decrease in the concentration of BTMACB at 394 nm for up to 80% reaction. No other reactant or product has any significant absorption at this wavelength. Pseudo-first-order rate constants, k_{obs}, were evaluated from linear plots ($r > 0.995$) of log[BTMACB] against time. Duplicate kinetic runs showed that the rate constants are reproducible to within $\pm$ 3%. The second-order rate constant, k_2, was determined from the relation: $k_2 = k_{obs}/$[hydroxy acid].

3. Results

Experimental data were obtained for all the hydroxy acids. Since the results are similar, only representative data are reproduced here.

3.1 *Stoichiometry*

The oxidation of hydroxy acids by BTMACB leads to the formation of corresponding oxoacids. The overall reaction may be written as:

$$RCH(OH)COOH + PhCH_2Me_3NBr_2Cl \rightarrow RCOCOOH + PhCH_2Me_3NCl + 2\,HBr. \qquad (1)$$
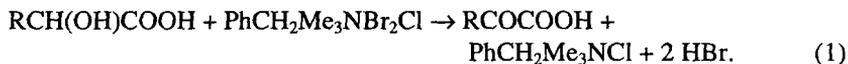
3.2 *Rate laws*

The reactions are of first order with respect to BTMACB. Further, the pseudo-first-order rate constant, k_{obs}, does not depend on the initial [BTMACB]. The reaction is first order with respect to the hydroxy acids also (table 1).

Table 1. Rate constants for the oxidation of mandelic acid by BTMACB at 303 K.

10^3[BTMACB] (mol dm^{-3})	[MA] (mol dm^{-3})	$10^4\,k_{obs}$ (s^{-1})
1·00	0·10	1·02
1·00	0·20	2·05
1·00	0·40	4·03
1·00	0·60	6·20
1·00	0·80	8·15
1·00	1·00	9·90
2·00	0·20	2·36
4·00	0·20	2·23
6·00	0·20	2·10
8·00	0·20	2·00
1·00	0·10	1·10*

*Contained 0·005 mol dm^{-3} acrylonitrile

Table 2. Effect of benzyltrimethylammonium chloride/bromide ion on the rate of oxidation of mandelic acid by BTMACB. [BTMACB] = 0·001 mol dm^{-3}, [MA] = 1·0 mol dm^{-3}, Temp. = 303 K

$10^4\,k_{obs}$/s^{-1} for (mol dm^{-3})	10^3[BTMACl] or [Br$^-$]				
	0·2	0·4	0·6	0·8	1·0
BTMACl	10·1	9·33	9·72	9·15	9·46
Br$^-$	9·36	9·81	9·10	10·2	9·00

3.3 *Induced polymerization of acrylonitrile*

Oxidation of the hydroxy acids in an atmosphere of nitrogen failed to induce the polymerization of acrylonitrile. Further, the addition of acrylonitrile had no effect on the rate of oxidation (table 1).

3.4 *Effect of benzyltrimethylammonium chloride or bromide ions*

Addition of benzyltrimethylammonium chloride (BTMACl) or bromide ions had no effect on the rate of oxidation (table 2).

3.5 *Kinetic isotope effect*

To ascertain the importance of the cleavage of the α-C–H bond in the rate-determining step, the oxidation of α-deuteriomandelic acid (DMA) was studied. Results showed the presence of a substantial primary kinetic isotope effect. The value of k_H/k_D at 303 K was 5·27.

3.6 *Solvent isotope effect*

The oxidation of mandelic acid was studied in 95% deuterium oxide under identical conditions. The results showed the absence of a solvent isotope effect. In this set of experiments, no acetic acid was present in the solvent.

Table 3. Effect of solvent composition in the oxidation of mandelic acid by BTMACB.
[BTMACB] = 0·001 mol dm^{-3}, [MA] = 1·0 mol dm^{-3}, Temp. = 303 K

	% AcOH				
	25	40	50	60	72
$10^4\,k_{obs}$ (dm^3 mol^{-1} s^{-1})	24·6	15·7	9·90	6·36	3·91

Table 4. Rate constants and activation parameters of the oxidation of substituted mandelic acids by BTMACB.

Subst.	$10^4\,k_2$/(dm^3 mol^{-1} s^{-1}) at				ΔH^* (kJ mol^{-1})	ΔS^* (J mol^{-1}K^{-1})	ΔG^* (kJ mol^{-1})
	293 K	303 K	313 K	323 K			
H	4·61	9·90	21·1	44·8	57·1 ± 0·7	−105 ± 2	91·1 ± 0·6
p-F	6·63	14·0	28·1	61·6	55·5 ± 1·2	−117 ± 4	90·2 ± 0·9
p-Cl	2·57	5·85	13·2	28·3	60·5 ± 0·4	−108 ± 1	92·5 ± 0·3
p-Br	2·10	4·85	10·6	24·0	61·1 ± 0·8	−107 ± 3	93·0 ± 0·6
p-Me	24·0	45·1	85·0	155	46·5 ± 0·5	−137 ± 2	87·2 ± 0·4
p-Pr^i	20·7	38·8	72·2	135	46·6 ± 0·7	−138 ± 2	87·5 ± 0·5
p-OMe	288	440	665	1050	31·2 ± 0·8	−168 ± 3	81·3 ± 0·6
m-Cl	0·63	1·68	4·35	9·92	70·1 ± 0·4	−87 ± 2	95·7 ± 0·4
m-NO$_2$	0·11	0·31	0·89	2·60	80·3 ± 1·4	−66 ± 5	99·9 ± 1·1
p-NO$_2$	0·08	0·23	0·71	1·90	81·0 ± 1·7	−66 ± 3	99·0 ± 0·8
GA	1·58	3·63	8·00	17·6	60·6 ± 0·5	−112 ± 2	93·7 ± 0·4
LA	2·86	6·34	14·1	31·2	60·1 ± 0·8	−108 ± 3	92·2 ± 0·7
MLA	2·22	5·00	11·1	25·3	61·1 ± 0·9	−107 ± 3	92·8 ± 0·8
DMA	0·83	1·88	4·10	8·93	59·7 ± 0·6	−120 ± 2	95·3 ± 0·4
k_H/k_D	5·55	5·27	5·15	5·02			

3.7 *Effect of solvent composition*

The rate of oxidation was determined in solvents of different amounts of acetic acid and water. It was observed that the rate of reaction increases with increase in the amount of water in the solvent mixture (table 3).

3.8 *Effect of temperature*

Rates for the oxidation of hydroxy acids were obtained at different temperatures and the activation parameters calculated (table 4).

4. Discussion

We have carried out some conductivity measurements to determine the nature of BTMACB in aqueous acetic acid solution. It was observed that acetic acid has very low conductivity. Addition of BTMACB increases the conductivity of acetic acid. We also measured the conductivity of BTMACB in solvents containing different proportions of acetic acid (100–30%) and water. We found that the conductivity initially increases sharply as the water content is increased but reaches a limiting value in about 60% acetic

acid–water mixture. Therefore, BTMACB can be considered as an ionic compound that exists under our reaction conditions as benzyltrimethylammonium and chlorobromate ions (2). The fact that added benzyltrimethylammonium ions have no effect also indicates that the equilibrium (2) lies far towards the right.

$$PhCH_2Me_3NBr_2Cl \rightleftharpoons PhCH_2Me_3N^+ + Br_2Cl^-. \qquad (2)$$

The following equilibria may also exist in solution:

$$Br_2Cl^- \rightleftharpoons Br_2 + Cl^-, \qquad (3)$$

$$Br_2 + H_2O \rightleftharpoons HOBr + HBr. \qquad (4)$$

The probable oxidizing species in a solution of BTMACB are, therefore, chlorobromate ions, molecular bromine and hypobromous acid. The equilibria (3) and (4) are likely to be suppressed by the addition of BTMACl or bromide ions. Chloride and bromide ions having no effect on the reaction rate rules out any role of Br_2 and HOBr in the oxidation process. Similar results were obtained in the oxidation of aldehydes by BTMACB [10]. Thus, in the present reaction also, the reactive oxidising species is the chlorobromate ion.

Values of the primary kinetic isotope effect ($k_H/k_D = 5.27$) are very close to the values obtained in the oxidation of mandelic acid by bromine [15] and pyridinium hydrobromide perbromide [16]. This confirms that the rate-determining step involves a cleavage of the α-C–H bond.

In deuterium oxide, active hydrogens, such as those present in hydroxyl and carboxyl groups, undergo rapid deuterium exchange resulting in the formation of –OD and –COOD groups. If a cleavage of the hydroxyl and/or carboxyl group is involved in the rate-determining step, the O–H–O–D kinetic isotope effect comes into play and the rate in D_2O should be less than that in H_2O. However, replacement of water by deuterium oxide has no effect on the oxidation rate pointing against the cleavage of hydroxyl and carboxyl groups in the rate–determining step. This is supported by the formation of the corresponding oxoacids as the main product.
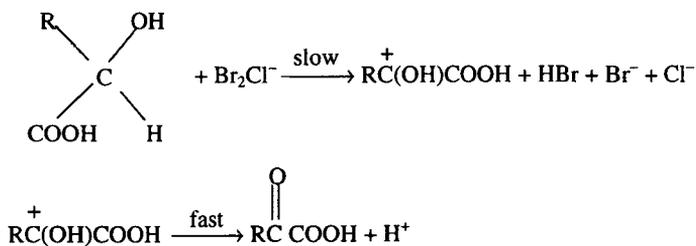
The increase in reaction rates with increase in the water content of the solvent mixtures showed that the species in the transition state in all the reactions are more polar than the reactants. The plot of $\log k_{obs}$ against the inverse of the dielectric constant is nonlinear. The solvent effect was analysed using the Winstein–Grunwald equation [17].

$$\log k = \log k_0 + mY. \qquad (5)$$

The plot of $\log k$ versus Y is linear ($r = 0.9995$) with $m = 0.89 \pm 0.02$. The value of m points to a transition state which is more polar than the reactants. Thus considerable charge separation takes place in the transition state of the reaction.

Table 5. Temperature dependence of the reaction constants.

Reaction constant	Temperature (K)			
	293	303	313	323
ρ^+	-2.29 ± 0.01	-2.11 ± 0.01	-1.91 ± 0.01	-1.76 ± 0.01
r^2	0.9998	0.9996	0.9997	0.9998
sd	0.01	0.02	0.02	0.01

$$R-C(OH)(COOH)(H) + Br_2Cl^- \xrightarrow{slow} \overset{+}{R}C(OH)COOH + HBr + Br^- + Cl^-$$

$$\overset{+}{R}C(OH)COOH \xrightarrow{fast} RC(=O)COOH + H^+$$

Scheme 1.

The rate of oxidation of substituted mandelic acids correlated well with Brown's σ^+ values[18], the reaction constant being negative (table 5). The correlation with Hammett's σ values was not very significant. The large negative reaction constants and correlation with σ^+ values indicate a carbocationic reaction centre in the transition state. This is supported by the observed large deuterium kinetic isotope effect. The mechanism depicted in scheme 1 accounts for all the observed data.

The negative entropy of activation also supports the above mechanism. When two reacting molecules combine to form a single activated complex, restrictions on their movement obviously increase, as they cannot move independently[19].

Acknowledgement

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