Oxidation of Some α-Hydroxy Acids by Tetraethylammonium Chlorochromate: A Kinetic and Mechanistic Study

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ABSTRACT: The oxidation of glycolic, lactic, malic, and a few substituted mandelic acids by tetraethylammonium chlorochromate (TEACC) in dimethylsulfoxide leads to the formation of corresponding oxoacids. The reaction is first order each in TEACC and hydroxy acids. Reaction is failed to induce the polymerization of acrylonitrile. The oxidation of α -deuteriomandelic acid shows the presence of a primary kinetic isotope effect ($k_H/k_D = 5.63$ at 298 K). The reaction does not exhibit the solvent isotope effect. The reaction is catalyzed by the hydrogen ions. The hydrogen ion dependence has the following form: $k_{obs} = a + b[H^+]$. Oxidation of *p*-methylmandelic acid has been studied in 19 different organic solvents. The solvent effect has been analyzed by using Kamlet's and Swain's multiparametric equations. A mechanism involving a hydride ion transfer via a chromate ester is proposed. © 2009 Wiley Periodicals, Inc. Int J Chem Kinet 42: 50–55, 2010

INTRODUCTION

Specific and selective oxidation of organic compounds under nonaqueous conditions is an important reaction in synthetic organic chemistry. For this, a number of different chromium(VI) derivatives have been reported [1–5]. Tetraethylammonium chlorochromate (TEACC) is one such compound used for the oxidation of primary aliphatic alcohols [6]. α -Hydroxy acids may be oxidized either as alcohols, yielding corresponding oxoacids [7], or they may undergo oxidative decarboxylation to yield a ketone [8]. There seems to be no report on the oxidation aspects using TEACC. We have been interested in the kinetic and mechanistic aspects of the oxidation by complexed Cr(VI) species, and several studies on halochromates have already been reported [9–12]. In continuation of our earlier work, we now report the kinetics of oxidation of some hydroxy acids by TEACC in DMSO as solvent. A suitable mechanism has also been proposed.

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EXPERIMENTAL

Materials

The hydroxy acids were commercial products (Merck, Ltd., Mumbai, India) of the highest purity available and were used as such. The preparation and specification of the substituted mandelic acids have been described earlier [13]. TEACC was prepared by the reported method [6], and its purity was checked by an iodometric method. α -Deuteriomandelic acid (PhCD(OH)COOH or DMA) was prepared by the method of Kemp and Waters [14]. Its isotopic purity, ascertained by NMR spectra, was 95 ± 4%. Because of the nonaqueous nature of the solvent, *p*-toluenesulfonic acid (TsOH) was used as a source of hydrogen ions. Solvents were purified by the usual methods.

Product Analysis

Product analyses were carried out under kinetic conditions, i.e., with an excess of the reductant over TEACC. In a typical experiment, mandelic acid (7.6 g, 0.05 mol) and TEACC (2.66 g, 0.01 mol) were dissolved in 100 mL of DMSO and was allowed to stand in dark for ≈ 24 h to ensure the completion of the reaction. It was then treated with an excess (250 mL) of a freshly prepared saturated solution of 2,4-dinitrophenylhydrazine in 2 mol dm^{-3} HCl and was kept overnight in a refrigerator. The precipitated 2,4-dinitrophenyl-hydrazone (DNP) was filtered off, dried, weighed, recrystallized from ethanol, and weighed again. The product was identical (mp and mixed mp) to an authentic sample of DNP of phenylglyoxylic acid. Similar experiments with the other hydroxy acids yielded the DNP of the corresponding oxoacids in 79%-88% yields after recrystallization. The oxidation state of chromium in completely reduced reaction mixtures, determined by an iodometric method, was 3.95 ± 0.10 .

Kinetic Measurements

The pseudo-first-order conditions were attained by keeping a large excess (×15 or greater) of the hydroxy acid over TEACC. The temperature was kept constant to ± 0.1 K. The solvent was DMSO, unless specified otherwise. The reactions were followed by monitoring the decrease in the concentration of TEACC spectrophotometrically at 350 nm for up to 80% of the reaction. No other reactant or product has any significant absorption at this wavelength. The pseudo-first-order rate constants, k_{obs} , were computed from the linear least-square plots of log[TEACC] versus time. Duplicate kinetic runs showed that the rates were

reproducible within $\pm 3\%$. The second-order rate constants, k_2 , were calculated from the following relationship: $k_2 = k_{obs}/[hydroxy acid]$. All experiments, other than those for studying the effect of hydrogen ions, were carried out in the absence of TsOH.

RESULTS

The rate and other experimental data were obtained for all the hydroxy acids studied. Since the results were similar, only representative data are reproduced here.

Stoichiometry

The oxidation of hydroxy acids resulted in the formation of the corresponding oxoacids. Product analysis and stoichiometric determinations indicated that the overall reaction could be written as

ArCH(OH)COOH +
$$O_2$$
CrClO⁻N⁺Et₄
 \rightarrow ArCOCOOH + H_2O + OCrCl O⁻N⁺Et₄ (1)

TEACC undergoes a two-electron change. This is according to the earlier observations with structurally similar other halochromates. It has already been shown that both pyridinium fluorochromate (PFC) [15] and pyridinium chlorochromate (PCC) [16] act as twoelectron oxidants and are reduced to chromium(IV) species by determining the oxidation state of chromium by magnetic susceptibility, ESR, and IR studies.

Rate Laws

The reactions are of first order with respect to TEACC. The individual kinetic runs were strictly first order to TEACC. Furthermore, the pseudo-first-order rate constant, k_{obs} , does not depend on the initial concentration of TEACC. The reaction rate increases linearly with an increase in the concentration of the hydroxy acids (Table I). Thus, the reaction is first order with respect to the hydroxy acids also.

Induced Polymerization of Acrylonitrile. The oxidation of hydroxy acids, by TEACC, in an atmosphere of nitrogen failed to induce the polymerization of acrylonitrile. Furthermore, addition of acrylonitrile had no effect on the rate (Table I). To further confirm the absence of free radicals in the reaction pathway, the reaction was carried out in the presence of 0.05 mol dm⁻³ of 2,6-di-*t*-butyl-4-methylphenol (butylated hydroxytoluene or BHT). It was observed that BHT was recovered unchanged, almost quantitatively.

$\frac{10^3 \text{ [TEACC]}}{(\text{mal dm}^{-3})}$	[HA] $(mal dm^{-3})$	$10^4 k_{\rm obs}$
		(8)
1.00	0.10	3.22
1.00	0.20	6.21
1.00	0.40	12.6
1.00	0.60	18.7
1.00	0.80	24.3
1.00	1.00	31.5
2.00	0.40	13.5
4.00	0.40	11.7
6.00	0.40	13.0
8.00	0.40	12.8
1.00	0.60	18.9 ^a

Table IRate Constants for the Oxidation of MandelicAcid by TEACC at 308 K

^{*a*}Contained 0.001 mol dm⁻³ acrylonitrile.

Effect of Acidity. The reaction is catalyzed by hydrogen ions. TsOH was used as a source of hydrogen ions. The hydrogen ion dependence has the following form (Table II):

$$k_{\rm obs} = a + b \left[{\rm H}^+ \right] \tag{2}$$

The values of a and b, for p-methylmandelic acid, are $3.05 \pm 0.10 \times 10^{-3} \text{ s}^{-1}$ and $5.65 \pm 0.17 \times 10^{-3} \text{ mol}^{-1} \text{ dm}^3 \text{ s}^{-1}$, respectively ($r^2 = 0.9964$).

Effect of Temperature. The rates of all the hydroxy acids were determined at four different temperatures, and activation parameters were calculated (Table III).

Kinetic Isotope Effect. To ascertain the importance of the cleavage of the C–H bond in the rate-determining step, the oxidation of DMA was studied. Results showed the presence of a substantial kinetic isotope effect (Table III). The value of $k_{\rm H}/k_{\rm D}$ is 5.63 at 298 K.

Effect of Solvents. The rate of oxidation of *p*-methylmandelic acid was determined in 19 different organic solvents. The choice of the solvents was limited by the solubility of TEACC and reaction with primary and secondary alcohols. There was no noticeable reaction with the solvents chosen. The kinetics was similar in all the solvents. The values of k_2 at 298 K are presented in Table IV.

DISCUSSION

Reactive Oxidizing Species

The observed hydrogen ion dependence suggests that the reaction follows two mechanistic pathways, one acid independent and other acid dependent. The acid catalysis may well be attributed to a protonation of TEACC to give a stronger oxidant and electrophile.

$$[O_2 CrClO^- N^+ Et_4] + H^+ \stackrel{\rightarrow}{\longleftarrow} [HO \stackrel{+}{Cr} OClO^- N^+ Et_4]$$
(3)

The formation of a protonated Cr(VI) species has earlier been postulated in the reactions of structurally similar 2,2-bipyridinium chlorochromate [9] and morpholinium chlorochromate [12].

Solvent Effect

The rate constants of oxidation, k_2 , in 18 solvents (CS₂ was not considered, as the complete range of solvent parameters was not available) were correlated in terms of the linear solvation energy relationship (4) of Kamlet et al. [17]

$$\log k_2 = A_0 + p\pi^* + b\beta + a\alpha \tag{4}$$

In this equation, π^* represents the solvent polarity, β the hydrogen bond acceptor basicities, and α is the hydrogen bond donor acidity. A_0 is the intercept term. The results of correlation analyses in terms of (4), a biparametric equation involving π^* and β , and separately with π^* and β , are given by

$$\log k_2 = -4.36 + (1.27 \pm 0.16)\pi^* + (0.16 \pm 0.14)\beta - (0.21 \pm 0.13)\alpha$$
(5)
$$R^2 = 0.8567; \text{ sd} = 0.15; n = 18; \Psi = 0.41$$

log
$$k_2 = -4.31 + (1.35 \pm 0.17)\pi^* + (0.09 \pm 0.14)\beta$$

 $R^2 = 0.8285; \text{ sd} = 0.16; n = 18; \Psi = 0.44$ ⁽⁶⁾

$$\log k_2 = -4.33 + (1.38 \pm 0.16)\pi^*$$

$$r^2 = 0.8240; \text{ sd} = 0.16; n = 18; \Psi = 0.43$$
(7)

log
$$k_2 = -2.90 + (0.33 \pm 0.30)\beta$$

 $r^2 = 0.0697$; sd = 0.36; $n = 18$; $\Psi = 0.99$ (8)

 Table II
 Effect of Hydrogen Ion Concentration on the Oxidation of p-Methylmandelic Acid by TEACC

$[TEACC] = 0.001 \text{ mol } dm^{-3}$		$[HA] = 1.00 \text{ mol } dm^{-3}$			Temperature = 308 K	
[H ⁺]	0.10	0.20	0.40	0.60	0.80	1.00
$10^4 k_{\rm obs}({\rm s}^{-1})$	36.0	42.3	54.0	62.1	76.5	87.3

	$10^4 k_2 (\mathrm{dm^3 \ mol^{-1} \ s^{-1}})$			ΔH^*	ΔS^*	ΔG^*	
R	288 K	298 K	308 K	318 K	$(kJ mol^{-1})$	$(J \text{ mol}^{-1} \text{ K}^{-1})$	$(kJ mol^{-1})$
Н	8.19	17.1	31.5	60.3	45.8 ± 0.7	-145 ± 2	88.8 ± 0.5
<i>p</i> -F	12.4	23.4	42.3	79.2	44.3 ± 0.6	-147 ± 2	88.0 ± 0.5
p-Cl	5.22	9.90	19.5	37.8	47.8 ± 1.9	-142 ± 3	90.1 ± 0.7
p-Br	4.32	8.28	16.4	31.5	48.0 ± 0.8	-143 ± 2	90.5 ± 0.6
p-Me	38.7	70.2	121	216	40.9 ± 0.5	-150 ± 2	85.3 ± 0.4
p-Pr ⁱ	33.3	61.2	108	189	41.4 ± 1.3	-149 ± 1	85.6 ± 0.2
p-OMe	360	585	936	1530	34.0 ± 0.6	-155 ± 2	80.0 ± 0.4
m-Cl	1.53	3.17	6.30	13.0	51.5 ± 0.8	-139 ± 3	92.9 ± 0.6
$m-NO_2$	0.30	0.67	1.44	3.15	56.9 ± 0.7	-134 ± 2	96.8 ± 0.5
$p-NO_2$	0.21	0.49	1.06	2.34	58.4 ± 0.5	-132 ± 2	97.6 ± 0.4
GA	3.87	7.11	13.0	24.3	44.0 ± 0.8	-158 ± 3	90.9 ± 0.6
LA	5.62	10.8	21.2	41.4	48.2 ± 0.8	-140 ± 3	89.9 ± 0.7
MLA	4.89	9.20	17.1	32.4	45.3 ± 0.7	-151 ± 2	90.3 ± 0.6
DMA	1.53	3.04	5.83	11.5	48.5 ± 0.7	-150 ± 2	93.1 ± 0.6
$k_{\rm H}/k_{\rm D}$	5.82	5.63	5.40	5.24			

 Table III
 Rate Constants and Activation Parameters for the Oxidation of Hydroxy Acids by TEACC

where *n* is the number of data points and Ψ is the Exner's statistical parameter [18].

Kamlet and coworkers' [17] triparametric equation explains ca. 86% of the effect of solvent on the oxidation. However, by Exner's criterion the correlation is not even satisfactory (cf. Eq. (5)). The major contribution is of solvent polarity. It alone accounted for ca. 82% of the data. Both β and α play relatively minor roles.

The data on the solvent effect were analyzed in terms of Swain and coworkers' equation [19] of cationand anion-solvating concept of the solvents also (9).

$$\log k_2 = aA + bB + C \tag{9}$$

where A and B represent the anion-solvating and cation-solvating power, respectively. C is the intercept term. (A + B) is postulated to represent the solvent polarity. The rates in different solvents were analyzed in terms of (9), separately with A and B and

with (A + B).

$$\log k_{2} = (0.38 \pm 0.03)A + (1.42 \pm 0.02)B - 4.07$$
(10)

$$R^{2} = 0.9960; \text{ sd} = 0.02; n = 19; \Psi = 0.07$$

$$\log k_{2} = 0.18(\pm 0.47)A - 2.85$$

$$r^{2} = 0.0081; \text{ sd} = 0.38; n = 19; \Psi = 1.02$$
(11)

$$\log k_{2} = 1.39(\pm 0.07)B - 4.29$$

$$r^{2} = 0.9587; \text{ sd} = 0.08; n = 19; \Psi = 0.21$$
(12)

$$\log k_{2} = 1.08 \pm 0.13(A + B) - 4.20$$

$$r^{2} = 0.7894; \text{ sd} = 0.18; n = 19; \Psi = 0.47$$
(13)

The rates of oxidation of p-methylmandelic acid in different solvents showed an excellent correlation in Swain's equation (cf. (10)) with the cation-solvating power playing the major role. In fact, the cation solvation alone accounts for ca. 96% of the data. The correlation with the anion-solvating power was very

Solvents	$10^4 k_2 (\mathrm{dm}^{-3} \mathrm{mol}^{-1} \mathrm{s}^{-1})$	Solvents	$10^4 k_2 (dm^{-3} mol^{-1} s^{-1})$
Chloroform	22.4	Toluene	9.77
1,2-Dichloroethane	30.9	Acetophenone	33.9
Dichloromethane	25.7	THF	14.8
DMSO	70.2	<i>t</i> -Butyl alcohol	10.7
Acetone	27.5	1,4-Dioxane	17.4
DMF	41.7	1,2-Dimethoxyethane	9.21
Butanone	19.5	Carbon disulfide	5.25
Nitrobenzene	30.2	Acetic acid	5.22
Benzene	12.0	Ethyl acetate	13.5
Cyclohexane	1.86	-	

 Table IV
 Effect of Solvents on the Oxidation of *p*-methylmandelic Acid by TEACC at 298 K

poor. The solvent polarity, represented by (A + B), also accounted for ca. 79% of the data.

Correlation Analysis of Reactivity

The reaction rates of substituted mandelic acids were correlated with Hammett's σ values but did not yield very significant correlation. The rates of oxidation of substituted mandelic acids correlated well with Brown and Okamoto's σ^+ values [20]. The reaction constant, ρ , has a value -2.07, -1.97, -1.89, and -1.80 at 288, 298, 308, and 318 K, respectively. The coefficient of correlation, r^2 , ranges from 0.9989 to 0.9999. The large negative reaction constants and correlation with σ^+ values indicate a carbocationic reaction center in the transition state.

Mechanisms

The absence of any effect of added acrylonitrile on the reaction discounts the possibility of a one-electron oxidation, leading to the formation of free radicals. The presence of a substantial kinetic isotope effect in the oxidation of mandelic acid confirms the cleavage of the α -C-H bond in the rate-determining step. The large negative reaction constant together with the excellent correlation with Brown and Okamoto's σ^+ values [20] points to a highly electron-deficient carbon center in the transition state. The transition state thus approaches a carbocation in character. This is supported by the solvent effect also. The greater role played by the cationsolvating power of the solvents supported the postulation of a carbocationic transition state. Therefore, the correlation analysis of substituent and solvent effects on the oxidation of mandelic acid supports the mechanism involving a hydride-ion transfer via either a chromate ester or a bimolecular reaction.

Kwart and Nickle [21] have shown that a study of the dependence of the kinetic isotope effect on temperature can be gainfully employed to resolve this problem. The data for protio- and deuteriomandelic acids, fitted to the familiar expression $k_{\rm H}/k_{\rm D} = A_{\rm H}/A_{\rm D} \exp(E_a/RT)$ [22,23], show a direct correspondence with the properties of a symmetrical transition state in which the activation energy difference (E_a) for $k_{\rm H}/k_{\rm D}$ is equal to the zero-point energy difference for the respective C–H and C–D bonds (≈4.5 kJ/mol) and the entropies of activation of the respective reactions are nearly equal. Similar phenomena were observed earlier in the oxidation of alcohols by quinolinium bromochromate [24] and that of hydroxy acids by PFC [25].

Bordwell [26] has documented a very cogent evidence against the occurrence of concerted one-step biomolecular processes by hydrogen transfer, and it is evident that in the present study also the hydrogen transfer does not occur by an acyclic biomolecular process. It is well established that intrinsically concerted sigmatropic reactions, characterized by transfer of hydrogen in a cyclic transition state, are the only truly symmetrical processes involving a linear hydrogen transfer [27]. Littler [28] has also shown that a cyclic hydride transfer, in the oxidation of alcohols by Cr(VI), involves six electrons and, being a Hückeltype system, is an allowed process. Thus the overall mechanism is proposed to involve the formation of a chromate ester in a fast pre-equilibrium and then a decomposition of the ester in a subsequent slow step via a cyclic concerted symmetrical transition state leading to the product (Schemes 1 and 2). The observed



Scheme 1 Acid-independent path.



Scheme 2 Acid-dependent path.

negative value of entropy of activation also supports a polar transition state. As the charge separation takes place, the charged ends become highly solvated. This results in an immobilization of a large number of solvent molecules, reflected in the loss of entropy [29].

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