

Kinetics and mechanism of oxidation of some α -hydroxy acids by quinolinium fluorochromate

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The oxidation of glycollic, lactic, malic and a few substituted mandelic acids by quinolinium fluorochromate (QFC) in ethyl sulphoxide (DMSO) leads to the formation of corresponding oxoacids. The reaction is first order each in QFC and the hydroxy acids. The reaction is catalysed by the hydrogen ions. The hydrogen ion dependence has the form: $k_{obs} = a + b [H^+]$. Oxidation of *p*-methylmandelic acid has been studied in 19 different organic solvents. The solvent effect has been analysed by using Kamlet's and Swain's multiparametric equations. A mechanism involving a hydride ion transfer via a chromate ester is proposed.

Quinolinium fluorochromate (QFC) has been used as an ideal selective oxidizing agent in synthetic organic chemistry¹. There are, however, not many reports available on the kinetic and mechanistic aspects of oxidation of hydroxy acids by QFC^{2,3}. We have been interested in kinetics of oxidation of hydroxy acids by Cr(VI) species and recently a few reports on re-oxidation by QFC have already been emanated from our laboratory⁴⁻⁷. Hydroxy acids may be oxidized to aldehydes or ketones, yielding corresponding oxoacids⁸ or undergo oxidative decarboxylation to yield a ketone. There seems to be no report on the oxidation of α -hydroxy acids by QFC. In continuation of our earlier work on QFC, we now report the kinetics and mechanism of oxidation of some hydroxy acids by QFC in DMSO solvent. A suitable mechanism has been proposed.

Materials and Methods

All hydroxy acids were commercial products of the highest purity available and were used as such. The synthesis and specification of the substituted mandelic acids have been described earlier¹⁰. QFC was prepared by the usual method¹ and its purity was checked by an analytical method. α -Deuteriomandelic acid

(TsOH) was used as a source of hydrogen ions. Solvents were purified by their usual methods¹².

Product analysis

Product analyses were carried out under kinetic conditions i.e., with an excess of the reductant over QFC. In a typical experiment mandelic acid (7.6 g, 0.05 mol) and QFC (2.13 g, 0.01 mol) were dissolved in 100 ml 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 kept overnight in a refrigerator. The precipitated 2,4-dinitrophenylhydrazone (DNP) was filtered off, dried, weighed, recrystallised 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 DNP of the corresponding oxoacids in 77 to 88% yield after recrystallization. The oxidation state of chromium in completely reduced reaction mixtures, determined by an iodometric method, was 3.91 ± 0.22 .

Kinetic measurements

wise. The reactions were followed by monitoring the decrease in the concentration of QFC spectrophotometrically at 365 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 $\log[QFC]$ 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 relation: $k_2 = k_{obs}/[\text{hydroxy acid}]$. All experiments, other than those for studying the effect of hydrogen ions, were carried out in the absence of TsOH.

Table 1- Rate constants for the oxidation of mandelic acid by QFC at 303 K

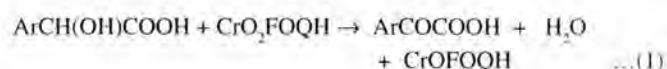
$10^3 [QFC]$ (mol dm ⁻³)	[HA] (mol dm ⁻³)	$10^4 k_{obs}$ (s ⁻¹)
1.00	0.10	1.21
1.00	0.20	2.38
1.00	0.40	4.72
1.00	0.60	7.16
1.00	0.80	9.53
1.00	1.00	11.9
1.00	2.00	24.4
2.00	0.20	2.30
4.00	0.20	2.45
6.00	0.20	2.33
8.00	0.20	2.52
1.00	0.40	4.85*

* Contained 0.001 mol dm⁻³ acrylonitrile

Results and Discussion

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.

The oxidation of hydroxy acids resulted in the formation of the corresponding oxoacids. Product analysis and stoichiometric determinations indicated that the overall reaction can be written as in Eq.1.



QFC undergoes a two electron change. This is in accord with our earlier observations with other halochromates¹³⁻¹⁴ as well as with QFC^{5,6}.

The reactions were found to be first order in QFC. The individual kinetic runs were strictly first order in QFC. Further, the pseudo-first order rate constant do not depend on the initial [QFC]. The reaction rate increases linearly with an increase in the [hydroxy acid](Table 1).

The oxidation of hydroxy acids, by QFC, in an atmosphere of nitrogen failed to induce the polymerisation of acrylonitrile. Further, an addition of acrylonitrile had no effect on the rate (Table 1). The reaction is catalysed by hydrogen ions. The hydrogen ion dependence has the following form (Table 2) :

$$k_{obs} = a + b [H^+] \quad \dots(2)$$

The values of a and b, for mandelic acid, are $1.20 \pm 0.01 \times 10^{-3} \text{ s}^{-1}$ and $2.11 \pm 0.01 \times 10^{-3} \text{ mol}^{-1} \text{ dm}^3 \text{ s}^{-1}$ respectively ($r^2 = 0.9993$).

The rates of oxidation of all the hydroxy acids were determined at four different temperatures and the activation parameters were calculated (Table 3).

To ascertain the importance of the cleavage of the C-H bond in the rate-determining step, the oxidation of α -deuterioformic acid (DMA) was studied. Results showed the presence of a substantial primary kinetic isotope effect. The value of k_H/k_D is 5.36 at 303 K. The oxidation of mandelic acid was studied in 95% deuterium oxide under identical conditions. The results showed the absence of a solvent isotope effect.

Table 2- Effect of hydrogen ion concentration on the oxidation of mandelic acid by QFC

[QFC] = 0.001 mol dm⁻³ ; [mandelic acid] = 1.0 mol dm⁻³ ; temp. = 303 K

[H ⁺]	0.10	0.20	0.40	0.60	0.80	1.00
$10^4 k_{obs}/\text{s}^{-1}$	14.1	16.3	20.5	24.0	29.1	33.1

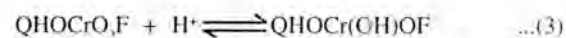
Table 3 - Rate constants and activation parameters for the oxidation of hydroxy acids by QFC

R	$10^4 k_2 / (\text{dm}^3 \text{mol}^{-1} \text{s}^{-1})$				ΔH^\ddagger (kJ mol ⁻¹)	ΔS^\ddagger (J mol ⁻¹ K ⁻¹)	ΔG^\ddagger (kJ mol ⁻¹)
	293	303	313	323 K			
H	6.32	11.9	23.6	43.3	48.4±0.7	-142±2	90.5±0.5
<i>p</i> -F	8.95	16.6	32.8	55.3	45.8±0.8	-147±3	89.6±0.7
<i>p</i> -Cl	3.61	7.10	14.4	29.2	52.3±0.9	-133±3	91.8±0.8
<i>p</i> -Br	3.02	5.92	12.7	24.0	52.5±0.9	-134±2	92.2±0.7
<i>p</i> -Me	29.8	50.5	88.8	152	40.3±0.7	-156±2	86.7±0.6
<i>p</i> -Pr ^t	24.0	42.2	76.7	124	41.0±0.6	-156±2	87.2±0.5
<i>p</i> -OMe	304	432	667	932	27.2±0.6	-182±2	81.2±0.4
<i>m</i> -Cl	1.02	2.15	4.83	9.31	55.6±0.6	-132±3	94.8±0.7
<i>m</i> -NO ₂	0.19	0.46	1.17	2.73	67.7±0.9	-105±3	98.8±0.7
<i>p</i> -NO ₂	0.13	0.32	0.85	2.00	69.7±0.9	-104±3	99.7±0.7
GA	2.25	4.16	7.75	14.8	46.8±0.9	-156±3	93.1±0.7
LA	4.15	8.11	15.8	31.4	50.4±0.9	-138±3	91.5±0.7
MLA	3.34	6.28	12.4	22.5	47.8±0.6	-149±2	92.0±0.5
DMA	1.15	2.22	4.54	8.65	50.7±0.8	-148±3	94.6±0.6
k_H/k_D	5.50	5.36	5.20	5.03			

The rate of oxidation of *p*-methylmandelic acid was determined in nineteen different organic solvents. The choice of the solvents was limited by the solubility of QFC and reaction with primary and secondary alcohols. There was no noticeable reaction with the solvents chosen. The kinetics were similar in all the solvents. The values of k_2 at 303 K are recorded in Table 4.

The entropy and enthalpy of activation of the oxidation of the ten substituted mandelic acids are linearly related ($r = 0.9818$). The value of isokinetic temperature evaluated^{15,16} from this plot is 1042±42 K. The correlation was tested and found genuine by using Exner's criterion¹⁷. A linear isokinetic relationship is necessary condition for the validity of linear free energy relationship, which suggests that all the hydroxy acids are oxidised by the same mechanism (Table 5).

The observed H⁺ dependence suggests that reaction follows two mechanistic pathways, one acid-independent and other acid-dependent. The acid catalysis may well be attributed to a protonation of QFC to give a stronger oxidant and electrophile.



The rate constants of oxidation, k_2 , in eighteen 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 [Eq.(4)] of Kamlet *et al.*¹⁸.

$$\log k_2 = A_0 + \rho\pi^* + b\beta + a\alpha \quad \dots(4)$$

In Eq.(4) π^* represents the solvent polarity, β the hydrogen bond acceptor basicities and α is the hydrogen

Table 4 - Effect of solvents on the oxidation of *p*-methyl mandelic acid by QFC at 303 K

Solvents	$10^4 k_2$ ($\text{dm}^3 \text{mol}^{-1} \text{s}^{-1}$)	Solvents	$10^4 k_2$ ($\text{dm}^3 \text{mol}^{-1} \text{s}^{-1}$)
Chloroform	14.5	Toluene	4.68
1,2-Dichloromethane	17.8	Acetophenone	20.9
Dichloromethane	15.8	THF	8.51
DMSO	50.5	<i>t</i> -Butyl alcohol	6.17
Acetone	16.6	1,4-Dioxane	7.94
DMF	25.7	1,2-Dimethoxyethane	4.37
Butanone	11.0	Carbon disulphide	2.29
Nitrobenzene	20.1	Acetic acid	2.69
Benzene	5.75	Ethyl acetate	6.31
Cyclohexane	0.62		

Table 5 - Temperature dependence of the reaction constant

Temp./ K	293	303	313	323
ρ^*	-2.15 ± 0.01	-2.00 ± 0.02	-1.85 ± 0.02	-1.71 ± 0.01
r^2	0.9999	0.9998	0.9989	0.9996
sd	0.001	0.007	0.008	0.018

bond donor acidity. A_0 is the intercept term. It may be mentioned here that out of the 18 solvents, 12 have a value of zero for α . The results of correlation analyses in terms of Eq.(4), a biparametric equation involving π^* and β , and separately with π^* and β are given below [Eqs (5 - 8)].

$$\log k_2 = -4.11 + (1.56 \pm 0.20) \pi^* + (0.19 \pm 0.16) \beta - (0.16 \pm 0.15) \alpha \quad \dots(5)$$

$$R^2 = 0.8569; \quad \text{sd} = 0.18; \quad n = 18; \quad \Psi = 0.30$$

$$\log k_2 = -4.14 + (1.62 \pm 0.19) \pi^* + (0.14 \pm 0.15) \beta \quad \dots(6)$$

$$R^2 = 0.8459; \quad \text{sd} = 0.17; \quad n = 18; \quad \Psi = 0.31$$

$$\log k_2 = -4.12 + (1.66 \pm 0.18) \pi^* \quad \dots(7)$$

$$r^2 = 0.8039; \quad \text{sd} = 0.17; \quad n = 18; \quad \Psi = 0.30$$

$$\log k_2 = -2.99 + (0.37 \pm 0.34) \beta \quad \dots(8)$$

$$r^2 = 0.0704; \quad \text{sd} = 0.43; \quad n = 18; \quad \Psi = 0.88$$

Here n is the number of data points and Ψ is the Exner's statistical parameter¹⁹.

Kamlet's¹⁸ 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. 8). The major contribution is of solvent polarity. It alone accounted for *ca.* 80% of the data. Both β and α play relatively minor roles.

The data on the solvent effect were analysed in terms of Swain's equation²⁰ of cation- and anion-solvating concept of the solvents also [Eq. (9)].

$$\log k_2 = aA + bB + C \quad \dots(9)$$

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

$$\log k_2 = (0.58 \pm 0.02) A + (1.69 \pm 0.01) B - 4.33 \quad \dots(10)$$

$$R^2 = 0.9990; \text{sd} = 0.02; n = 19; \Psi = 0.02$$

$$\log k_2 = 0.34(\pm 0.56) A - 3.16 \quad \dots(11)$$

$$r^2 = 0.0212; \text{sd} = 0.45; n = 19; \Psi = 0.95$$

$$\log k_2 = 1.65(\pm 0.10) B - 4.14 \quad \dots(12)$$

$$r^2 = 0.9376; \text{sd} = 0.11; n = 19; \Psi = 0.18$$

$$\log k_2 = 1.32 \pm 0.14 (A + B) - 4.29 \quad \dots(13)$$

$$r^2 = 0.8349; \text{sd} = 0.19; n = 19; \Psi = 0.30$$

The rates of oxidation of *p*-methylmandelic acid in different solvents showed an excellent correlation in Swain's equation [cf. Eq.(9)] with the cation-solvating power playing the major role. In fact, the cation-solvation alone accounts for *ca* 99% of the data. The correlation with the anion-solvating power was very poor. The solvent polarity, represented by (A + B), also accounted for *ca*. 83 % of the data. In view of the fact that solvent polarity is able to account for *ca*. 83 % of the data, an attempt was made to correlate the rate with the relative permittivity of the solvent. However, a plot of $\log k_2$ against the inverse of the relative permittivity is not linear ($r^2 = 0.5232$; $\text{sd} = 0.31$; $\Psi = 0.54$).

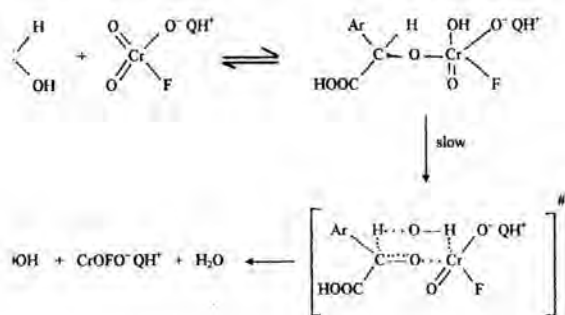
Mechanisms

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^{21,22} 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's σ^+ values²³ point to a highly electron-deficient carbon centre in the transition state. The transition state thus approaches a carbocation in character. This is supported by the solvent effect also. Greater role played by the cation-solvating 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 from hydroxy acid to QFC. The hydride ion transfer may take place either directly or via a chromate ester.

Kwart and Nickle²⁴ 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 $k_H/k_D = A_H/A_D \exp(\Delta E_0/RT)$ ^{25,26} show a direct correspondence with the properties of a symmetrical transition state in which the activation energy difference (ΔE_0) for k_H/k_D is equal to the zero-point energy difference for the respective C-H and C-D bonds (≈ 4.5 kJ/mol) and the frequency factors and the entropies of activation of the respective reactions are nearly equal. Similar phenomena were observed earlier in the oxidation of diols by BPCC²⁷ and that of hydroxy acids by PFC^{21,22}.

Bordwell²⁸ 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 studies 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 transfer²⁹. Littler³⁰ has also shown that a cyclic hydride transfer, in the oxidation of alcohols by Cr(VI), involves six electrons and, being a Huckel-type 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 (Scheme 1). The observed negative value of entropy of activation also supports a polar transition state.



Scheme 1

observed negative entropy of activation also supports the charge separation takes place, the charged complex is highly solvated. This results in an immobilization of a large number of solvent molecules, resulting in the loss of entropy³¹.

It is of interest to compare the mode of oxidation of α -hydroxy acids by PCC³², PFC²¹ and QFC. The oxidation by QFC exhibited a Michaelis-menten type kinetics with respect to hydroxy acids. While the oxidation by PCC and PFC presented a similar kinetic picture. The rate dependence on hydrogen ion concentration was similar in both the cases. In the oxidations by PCC and PFC excellent correlations were obtained in the form of Swain's equation with the cation solvating power of solvents playing the major role. In all the three cases the polar reactions are negative.

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