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Kinetics of the Oxidative Cleavage of α-Keto Acids by Quinolinium Bichromate[1]

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Abstract—Reaction rates for the quinolinium dichromate oxidation of α-ketoacids (pyruvic and phenylpyruvic) are determined and discussed with reference to ketoacid hydration equilibria. The rate of the reaction is dependent on the first powers of the concentrations of each (substrate, oxidant, and acid). The effect of variations in solvent composition (water-dimethylformamide mixtures) and temperature are studied. The effect of solvent is analyzed. The mechanistic pathway involves the rate-determining step of oxidative decomposition of the chromate ester of the hydrated form of the α-ketoacids and oxidative decarboxylation and a simultaneous cleavage of the carbon–carbon bond.

INTRODUCTION

The oxidation of pyruvic acid by various oxidants such as manganese(III) [1], cerium ions [2], iodine [3], permanganate [4], hexacyanoferrate(III) in an alkaline medium [5, 6], periodate [7], and vanadium(V) [8] has been reported. In our continuing efforts to use quinolinium dichromate [QDC, $(C_9H_7NH^+)_2Cr_2O_7^{2-}$] for the oxidation of organic substrates [9], this paper presents the kinetic features of the oxidation of α-ketoacids (pyruvic acid and phenylpyruvic acid) by QDC in an acid medium in a nitrogen atmosphere using 20% dimethylformamide as the solvent. This study was taken up to explore the efficiency of QDC in cleaving the carbon–carbon bond of these substrates. A mechanistic pathway for the oxidation reaction, consistent with the kinetic data has been suggested.

EXPERIMENTAL

(a) Materials

Pyruvic acid (Merck) and phenylpyruvic acid (Fluka) were used after distillation and recrystallization, respectively. Quinolinium dichromate (QDC) was prepared by the reported method [10], and its purity was checked by spectral analysis. The infrared spectrum (KBr) exhibited bands at 930, 875, 767, and 730 cm^{-1}, which is characteristic of the dichromate ion. Perchloric acid (Merck) was used after a check of its physical constants. Dimethylformamide (DMF) was distilled under reduced pressure and fraction distilling at 153°C was used. Doubly distilled water was used to prepare all solutions. The IR spectra were recorded on an FT-IR (DA-8, Bomen) spectrophotometer, and NMR spectra were recorded on an FT-NMR (300 MHz, Bruker) spectrometer.

(b) Kinetic measurements

Pseudo-first-order conditions were used (large excess of substrate over QDC). The reactions were carried out at a constant temperature (±0.1 K) and followed by monitoring the absorption band at 440 nm spectrophotometrically (Beckman DU 650, USA), as described in earlier papers [9]. The rate constants were evaluated from the linear plots ($r > 0.996$) of log [QDC] against time. The values reported in Tables 1–3 were the mean of two or more runs (accuracy, ±3%). The reactions were carried out in 20% aqueous DMF, and water–DMF mixtures were used for studying the effect of the dielectric constant on the rates of the reactions. All reactions were performed in a nitrogen atmosphere.

(c) Product analysis

A solution of substrate (0.01 mol/l) was mixed with QDC solution (0.02 mol/l) in the presence of perchloric acid (0.08 mol/l) in a 20% aqueous–DMF medium at 40°C. The reaction mixture was stirred in a nitrogen atmosphere for 24 h for the completion of the reaction.

Table 1. Rate data for the oxidation of α-ketoacids by QDC at 313 K

[QDC] × 10^3, mol/l	$k \times 10^5$, s^{-1}	
	pyruvic acid	phenylpyruvic acid
0.10	2.72	0.93
0.25	2.66	0.99
0.50	2.76	0.91
0.75	2.70	0.89
1.0	2.73	0.95

Note: [HClO$_4$] = 0.1 mol/l, [α-keto acid] = 5.0 × 10^{-3} mol/l, solvent = 20% DMF (%, vol/vol).

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[1] This article was submitted by the authors in English.

The evolution of CO_2 was observed. The organic layer was extracted with ether, washed with water, and dried over anhydrous Na_2SO_4. The oxidized products (acetic acid from pyruvic acid and phenylacetic acid from phenylpyruvic acid) were obtained after the complete removal of ether. Each of the reaction products obtained was subjected to IR (CCl_4) and NMR ($CDCl_3$; Me_4Si) analyses, and characterized as follows:

(i) Acetic acid:

IR: ν 3030 (br s, -OH), 1717 (s, C=O), 1414, 1361, 1291, 941, 619 cm^{-1}.

^1H NMR: δ 8.9 (s, 1H, 1-H), 2.2 (s, 3H, 2-H_3).

^{13}C NMR: δ 165.8 (C-1), 14.9 (C-2).

(ii) Phenylacetic acid:

IR: ν 2940 (br s, -OH), 1700 (s, C=O), 1520, 1410, 1350, 1280, 1240, 1190, 1030, 930, 680 cm^{-1}.

^1H NMR: δ 11.2 (s, 1H, 1-H), 8.1 (d, 2H, 4-H_2), 7.6 (t, 2H, 5-H_2), 7.5 (t, 1H, 6-H), 3.6 (s, 2H, 2-H_2).

^{13}C NMR: δ 171.4 (C-1), 133.3 (C-3), 129.7 (C-4), 129.1 (C-5), 128.6 (C-6), 16.4 (C-2).

RESULTS AND DISCUSSION

The oxidation of pyruvic acid and phenylpyruvic acid by QDC in an acid medium resulted in the formation of acetic acid and phenylacetic acid, respectively. Under the present experimental conditions, there was no further oxidation of the products.

Stoichiometry. The stoichiometry of the reaction was determined [9]. A stoichiometric Δ[QDC]/Δ[α-ketoacid] ratio of 0.67 was obtained suggesting the overall equation

$$\begin{aligned} &3RCOCO_2H + 2Cr(VI) + 3H_2O \\ &\longrightarrow 3RCO_2H + 3CO_2 + 2Cr(III) + 6H^+, \end{aligned} \qquad (I)$$

where R = CH_3 (pyruvic acid) and $C_6H_5CH_2$ (phenylpyruvic acid), respectively.

Rate law. Under pseudo-first-order conditions, the reactions exhibited a first-order dependence in [QDC], as seen from the constant values of k for a tenfold variation of [QDC] (Table 1). A tenfold variation of [substrate] showed a proportional increase in the rate constant. The plots of k versus [substrate] were linear passing through the origin, thereby confirming a first-order dependence on [substrate] (figure). The order dependence with respect to perchloric acid was unity (Table 1). A linear increase in the rate with acidity suggested the involvement of a protonated Cr(VI) species in the rate-determining step of the reaction. The acid catalysis must be related to the structure of the oxidant (QDC), which was converted into a protonated species at the concentrations of mineral acid used. Quinolinium dichromate is a bimetallic species, an anionic condensed form of chromic acid. The reactive form of the oxidant was characterized in the preceding paper [11]. The observed rate law is

$$w = k'[\text{substrate}][\text{QDC}][H^+]. \qquad (1)$$

Effect of temperature. A linear correlation between $\log k$ and the reciprocal temperature in the range 303–323 K was observed. The rate of the reaction was found to increase with an increase in the temperature. The rate data and activation parameters are shown in Table 2. The negative values of $\Delta S^{\neq}$ provided support for the formation of a rigid activated complex. The constancy in $\Delta G^{\neq}$ values suggested that a common mechanism was applicable for the oxidation of these substrates.

Effect of solvent. The oxidation of α-ketoacids by QDC was studied in solutions containing varying proportions of water and DMF. The dielectric constants for H_2O–DMF mixtures were estimated from the dielectric constants of the pure solvents [12]. It was observed that an increase in water content of the medium showed an increase in the rate of oxidation (Table 3). The absence of any salt effects on the rate of oxidation indicated that the reaction was not of the ion–ion type. The effect of solvent was analyzed in terms of its ionizing power, where Y represents a measure of the ionizing power of the solvent [13] defined by the equation

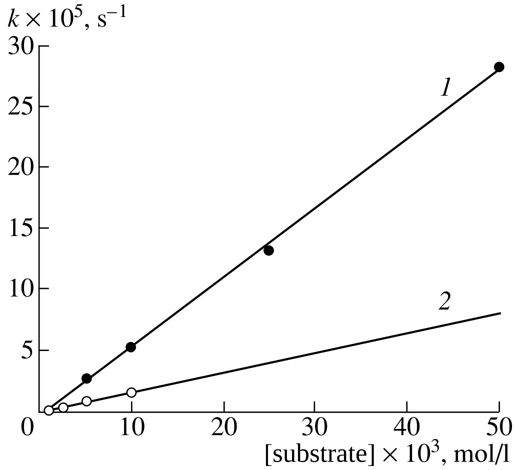
$$Y = \log k(H_2O) - \log k_0(H_2O). \qquad (2)$$

Here $k_0(H_2O)$ and $k(H_2O)$ are the rate constants of α-ketoacids at 40°C in 80% water and in successive solvent mixtures (water–DMF), respectively. Using this definition, Y is zero in 80% water, and Y varies for the solvent range used (Table 3). The variation of the solvolysis rate constant k with the solvent gives a linear free energy relation [13], where m represents the parameter measuring the sensitivity of the solvolysis rate to Y. The values of $\log k_0$ are shown in Table 3; $m = 1$ suggests that the passage to the transition state involved an increase in charge. This could be attributed to a progressive increase in solvation in going from the

Table 2. Temperature and activation parameters for oxidation of α-ketoacids by QDC

	$T \pm 0.1$, K	Pyruvic acid	Phenylpyruvic acid
$k \times 10^5$, s^{-1}	303	1.23	0.39
	308	1.90	0.62
	313	2.73	0.95
	318	4.07	1.32
	323	5.62	2.24
E_a, kJ mol^{-1}	–	63 ± 2	71 ± 2
$\Delta H^{\neq}$, kJ mol^{-1}	–	59 ± 2	67 ± 2
$\Delta S^{\neq}$, J K^{-1} mol^{-1}	–	–144 ± 3	–129 ± 3
$\Delta G^{\neq}$, kJ mol^{-1}	–	102 ± 1	105 ± 1

Note: [α-Keto acid] = 5.0×10^{-3} mol/l, [QDC] = 1.0×10^{-3} mol/l, [$HClO_4$] = 0.1 mol/l, solvent—20% DMF (%, vol/vol).



Plots of k vs. [substrate], [QDC] = 1.0×10^{-3} mol/l; [$HClO_4$] = 0.1 mol/l; [DMF] = 20%(vol/vol); T = 313 K. (*1*) Pyruvic acid, (*2*) phenylpyruvic acid.

reactants to the transition state. Hence, a change to a more strongly ionizing medium (from 65% H_2O to 100% H_2O) resulted in an increase in the rate of the reaction (Table 3).

Mechanism. It has been shown that the oxidation of pyruvic acid by manganese pyrophosphate did not proceed by enolization, but by a cyclic intermediate which was kinetically detectable and which underwent homolytic fission to yield a radical; the acyl radical reacted further to form acetic acid [14]. The oxidation of pyruvic acid by vanadium(V) was shown to proceed through the formation of free radical intermediates indicating that vanadium(V) underwent one-electron reduction [15, 16]. In the present investigation, the addition of acrylonitrile to the reaction mixture did not result in any polymerization, and the addition of mercury (II) chloride did not result in any reduction [17]. This indicated that QDC did not behave as a one-equivalent oxidant.

It has been shown that α-ketoacids are hydrated in aqueous solution [18–20].

Pyruvic acid is a strong organic acid with the value of $K_a = 3.2 \times 10^{-3}$ at 25°C [18, 19, 21] and a hydration constant $K_h = 3.1$. Consequently, in the pH range studied, the extent of hydration of pyruvic acid increases. Thus, the hydrated form of pyruvic acid would remain as an undissociated molecule (since $[H^+] \gg K_a$) in the range of acid concentrations used in this study (0.05–0.25 mol/l). It is, therefore, suggested that QDC reacts with the hydrated form of the α-ketoacids. In this investigation, it was observed that QDC reacts quantitatively with pyruvic acid to give acetic acid and CO_2 (and with phenylpyruvic acid to give phenylacetic acid and CO_2). Consequently, the corresponding enol, $CH_2{=}C(OH)COOH$, which (by analogy with the enolic forms of simple ketones) should be more extensively oxidized, does not appear to be involved.

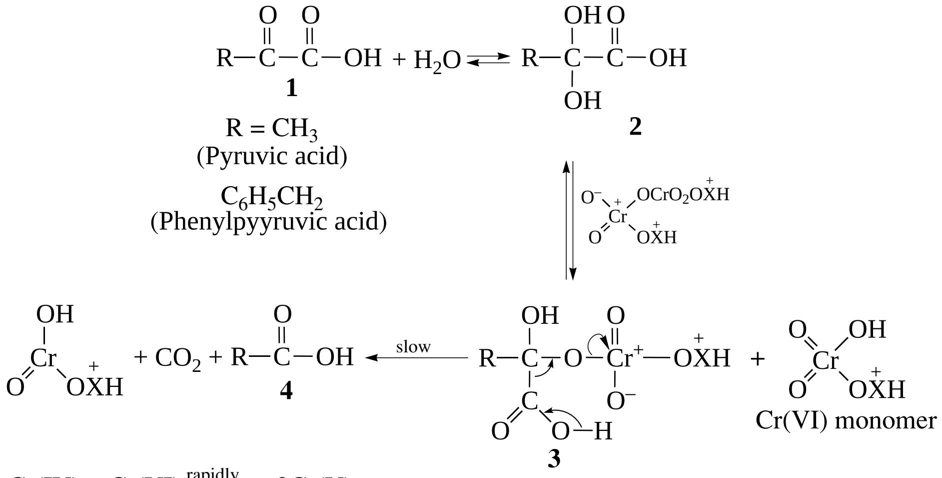
The order of reactivity observed for the oxidation of α-ketoacids was pyruvic acid > phenylpyruvic acid (Table 1), showing that the +I effect of the methyl group (in pyruvic acid) was predominant over the –I effect of the benzyl group (in phenylpyruvic acid). The activation parameters obtained indicated that the activation energy was much less for the oxidation of pyruvic acid than for phenylpyruvic acid. Furthermore, the presence of an electron-releasing group (as in pyruvic acid) accelerated the oxidation process by increasing the electron availability at the oxygen atom of the carbonyl group. This facilitated the attack of the electrophile (protonated QDC) on the hydrated form of the α-ketoacids. The net result was that the rupture of the carbon–carbon bond in pyruvic acid occurred more easily than that in phenylpyruvic acid, which explains the observed order of reactivity.

All the experimental results would suggest a mechanistic pathway for the oxidation reaction as shown in

Table 3. Solvent effect for oxidation of α-ketoacids by QDC at 313 K

Compound	H_2O : DMF (%, vol/vol)	D	$k \times 10^5$, s^{-1}	$\log k_0$	Y
Pyruvic acid	100 : 0	73.3	7.24	–4.56	0.42
	95 : 5	71.5	6.52		0.37
	90 : 10	69.7	5.21		0.28
	85 : 15	67.9	4.03		0.17
	80 : 20	66.2	2.73		0
Phenylpyruvic acid	85 : 15	67.9	1.02	–5.02	0.03
	80 : 20	66.2	0.95		0
	75 : 25	64.4	0.84		–0.06
	70 : 30	62.6	0.71		–0.13
	65 : 35	60.8	0.54		–0.25

Note: [α-keto acid] = 5.0×10^{-3} mol/l, [QDC] = 1.0×10^{-3} mol/l, [$HClO_4$] = 0.1 mol/l.



$$Cr(IV) + Cr(VI) \xrightarrow{\text{rapidly}} 2Cr(V)$$

$$Cr(V) + \text{substrate} \xrightarrow{\text{rapidly}} \text{Product} + Cr(III)$$

X—Quinolinium

Scheme 1.

the Scheme 1. The mechanistic pathway of the reaction under consideration could be summarized as follows: (a) in the first step of the reaction, α-ketoacids **1** in water forms the hydrate **2**; (b) the reaction of **2** with the oxidant (QDC) gives the chromate ester **3**; (c) the ester **3** undergoes decomposition in the slow step to yield the product **4** identified as acetic acid (from pyruvic acid) and phenylacetic acid (from phenylpyruvic acid) with the evolution of carbon dioxide. The oxidation reaction thus takes place by the rupture of the carbon–carbon bond. The formation of acetic acid would be expected only when the hydrated form of pyruvic acid acts as a reducing substrate [22, 23]. On the other hand, if it were to be suggested that the pyruvic acid underwent enolization and not hydration, then the product obtained would be oxalic acid (and not acetic acid, as obtained in the present study). Hence, the enolization of α-ketoacids is ruled out.

The conversion of Cr(IV) to Cr(III) is a disproportionation reaction. For the reaction $Cr(IV) + Cr(VI) \longrightarrow 2Cr(V)$, the standard potential for the Cr(VI)–Cr(V) couple is extremely favorable (E_0 = 0.62 V), and this reaction would proceed rapidly [24]. The Cr(V)–Cr(III) couple has a potential of 1.75 V, which would facilitate the rapid conversion of Cr(V) to Cr(III) after the reaction with the substrate [24, 25].

This kinetic investigation has demonstrated the utility of QDC in the oxidation of α-ketoacids, wherein there was a cleavage of the carbon–carbon bond in the final step of the reaction. This study further emphasizes the utility of QDG as an oxidant that can be used for the cleavage of α-ketoacids.

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