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Mechanism of the oxidative ketones by quinolinium dichromate

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Abstract

The kinetics of the oxidation of ketones (cyclic and arylalkyl) by quinolinium dichromate (QDC), in an acid medium, has been investigated. The rate of the reaction was proportional to the concentrations of the ketone, QDC, and acid. The order of reactivity for the cyclic ketones was $C_6 > C_8 > C_5 > C_7$ (ring size) and acetophenone > propiophenone > butyrophenone > valerophenone (arylalkyl ketones). A kinetic isotope effect, $k_H/k_D = 5.80$, was observed (cyclohexanone and cyclohexanone–d_4). The rate data have been rationalized using conformational considerations. The mechanism involved the attack of the protonated QDC on the enol form (of the ketone), in the rate-determining step, forming a cyclic chromate ester. Subsequent cleavage of the carbon–carbon bond of the ester yielded carboxylic acids as the products.

Introduction

Since there exists an equilibrium between the keto form and the enol form of ketones, different views have been expressed on either the keto form [1–3] or the enol form [4–7] undergoing reactions with different oxidants. The correlations that have emerged from these studies are the following:

(a) when carboxylic acids were the major products, the oxidation was through a rate-determining attack of the oxidant on the enol form of the ketone, as in oxida- tions with acid permanganate [8, 9], chloramine-T [10], and acidic potassium bromate [11];

(b) when diketones were formed, the rate-determin- ing step involved the reaction between the protonated form of the ketone and the oxidant, as in the oxidation with N-bromosaccharin [12]; and

(c) when a methoxy derivative was the final product, there was the rate-determining attack of the oxidant on the enol form of the ketone leading to the formation of an intermediate carbocation, as in the oxidation with acid iodate [13].

Confronted with all these possibilities, we have used kinetic data to ascertain which of these mechanisms was prevalent in the oxidation reactions of ketones. For this purpose, we have studied the

kinetics of oxidation of cyclic ketones (cyclopentanone, cyclohexanone, cycloheptanone, and cyclooctanone) and arylalkyl ketones (acetophenone, propiophenone, butyrophenone, and valerophenone) by quinolinium dichromate [QDC,(C9H7NH+)2Cr2] in an acid medium. This investigation was carried out to determine whether QDC was capable of cleaving the ring system (of cyclic ketones) and of cleaving the carbon–carbon bond (of arylalkyl ketones) and also to look for correlations between structure and reactivity which would help to decipher the mechanism of the oxidation of these ketones. This study forms part of our sustained efforts to exploit QDC for the oxidation of organic substrates in general [14], and it is the first kinetic report of the use of a complexed chromium (VI) reagent for the oxidation of cyclic and arylalkyl ketones.

Experimental

Materials, methods and stoichiometry

Cyclopentanone and cyclohexanone (E. Merck) were used after distillation. Cycloheptanone and cyclooctanone (Fluka) were used after distillation and recrystallization, respectively. Acetophenone (E. Merck), propiophenone (Spectrochem), and butyrophenone and valerophenone (Aldrich) were all distilled before use. Quinolinium dichromate (QDC) was prepared by the reported method [15]; the infrared spectrum (KBr) exhibited bands at 930, 875, 765 and 730 cm^{-1}, which are characteristic of the dichromate ion. Sulfuric acid and perchloric acid (E. Merck) were used after a check of their physical constants. Acetic acid (E. Merck) was distilled, and the fraction distilling at 116°C was used. Dimethylformamide (Spectrochem) was distilled under reduced pressure, and the fraction distilling at 153°C was used. The IR spectra were recorded on a FT–IR (DA–8, Bomen) spectrophotometer, and the NMR spectra, on an FT–NMR (300 MHz, Bruker) spectrometer.

Pseudo–first-order conditions were used ([substrate] ≫ [QDC]), and the reactions (performed at constant temperature) were followed by monitoring the disappearance of Cr(VI) at 440 nm (Beckman DU 650), as described in earlier papers [14]. Rate constants were evaluated from the linear ($r > 0.996$) plots of log [QDC] against time. The values of the rate constants reported were the mean of two or more kinetic runs (reproducibility ± 3%). All reactions were performed under a nitrogen atmosphere.

The stoichiometrics of the reactions were determined [14] to be

$$C_6H_{10}O + 2Cr^{VI} + 3H_2O \rightarrow C_6H_{10}O_4 + 2Cr^{III} + 6H^+,$$

$$C_6H_5COCH_2R + 2Cr^{VI} + 3H_2O \rightarrow C_6H_5CO_2H + RCO_2H + 2Cr^{III} + 6H^+$$

[R = –H (acetophenone), $–CH_3$ (propiophenone), $-C_2H_5$ (butyrophenone), and $–C_3H_7$ (valerophenone)], respectively.

Product Analysis

Using the same experimental conditions as were used for the kinetic determinations, the reaction mixture was stirred for 48 h under nitrogen. The organic layer was extracted with ether (3 × 25 ml), and the combined

organic extracts were washed with water, and dried over anhy- drous Na_2SO_4. The ether was removed by warming, and the product obtained was recrystallized from hot water. The products obtained (yields ≈85–90%) from the oxidation of cyclic ketones (glutaric acid from cyclopentanone, adipic acid from cyclohexanone, pimelic acid from cyclo- heptanone, and suberic acid from cyclooctanone) and from the oxidation of arylalkyl ketones (yields: ≈80–85% benzoic acid; ≈7–10% aliphatic acid) were subjected to IR (KBr) and NMR ($CDCl_3$/1 drop DMSO–d_6; Me_4Si) analyses and characterized as follows:

(i) Glutaric acid: IR, ν (cm^{-1}): 2940, 1690, 1470, 1305, 1265, 1205, 1065, 920, 760;
^{1}H NMR, δ: 5.5 (br s, 2H), 2.4 (t, 4H), 1.7 (m, 2H);
^{13}C NMR, δ: 175.5, 33.2, 20.1.

(ii) Adipic acid; IR, ν (cm^{-1}): 2950, 1725, 1460, 1430, 1410, 1280, 930, 735;
^{1}H NMR, δ: 6.8 (br s, 2H), 2.4 (t, 4H), 1.7 (m, 4H);
^{13}C NMR, δ: 176.0, 33.8, 24.4.

(iii) Pimelic acid; IR, ν (cm^{-1}): 2935, 1665, 1470, 1405, 1270, 1200, 915, 730;
^{1}H NMR, δ: 5.5 (br s, 2H), 2.4 (t, 4H), 1.7 (m, 4H), 1.4 (m, 2H);
^{13}C NMR, δ: 175.4, 33.9, 28.5, 24.5.

(iv) Suberic acid, IR, ν (cm^{-1}): 2940, 1695, 1425, 1330, 1250, 1190, 930, 725;
^{1}H NMR, δ: 6.7 (br s, 2H), 2.4 (t, 4H), 1.7 (m, 4H), 1.4 (m, 4H);
^{13}C NMR, δ: 175.9, 34.0, 28.6, 24.6.

(v) Benzoic acid and formic acid (*from acetophenone*).
^{1}H NMR, δ: 8.3 (c, 1H, 1-$H_{benzoic\ acid}$, 8.2 (c, 1H, 1-$H_{formic\ acid}$), 8.0 (d, 2H, 2-$H_{2,\ benzoic\ acid}$), 7.8 (s, 1H, 2-$H_{formic\ acid}$), 7.6 (t, 2H, 2-$H_{2,\ benzoic\ acid}$), 7.5 (t, 1H, 4-$H_{benzoic\ acid}$).
^{13}C NMR, δ: 170.6 ($C1_{benzoic\ acid}$, 165.5 ($C1_{formic\ acid}$), 134.1 ($C2_{benzoic\ acid}$), 130.2 ($C3_{benzoic\ acid}$), 129.6 ($C4_{benzoic\ acid}$), 128.9 ($C5_{benzoic\ acid}$).

(vi) Benzoic acid and acetic acid (*from propiophenone*):
^{1}H NMR, δ: 11.2 (s, 1H, 1-$H_{benzoic\ acid}$), 8.1 (d, 2H, 2-$H_{2,\ benzoic\ acid}$), 7.6 (t, 2H, 3-$H_{2,\ benzoic\ acid}$), 7.5 (t, 1H, 4-$H_{benzoic\ acid}$), 7.3 (s, 1H, 1-$H_{acetic\ acid}$), 2.1 (s, 1H, 2-$H_{3,\ acetic\ acid}$).
^{13}C NMR, δ: 177.3 ($C1_{acetic\ acid}$), 171.4 ($C1_{benzoic\ acid}$), 133.3 ($C2_{benzoic\ acid}$), 129.7 ($C3_{benzoic\ acid}$), 129.1 ($C4_{benzoic\ acid}$), 128.6 ($C5_{benzoic\ acid}$), 19.7 ($C2_{acetic\ acid}$).

(vii) Benzoic acid and propionic acid (*from butyrophenone*):
^{1}H NMR, δ: 11.6 (s, 1H, 1-$H_{benzoic\ acid}$), 10.6 (s, 1H, 1-$H_{propionic\ acid}$), 8.1 (d, 2H, 2-$H_{2,\ benzoic\ acid}$), 7.6 (t, 2H, 3-$H_{2,\ benzoic\ acid}$), 7.4 (t, 1H, 4-$H_{benzoic\ acid}$), 2.4 (q, 2H, 2-$H_{2,\ propionic\ acid}$), 1.1 (t, 3H, 3-$H_{3,\ propionic\ acid}$).
^{13}C NMR, δ: 181.4 ($C1_{propionic\ acid}$), 172.4 ($C1_{benzoic\ acid}$), 133.9 ($C2_{benzoic\ acid}$), 130.3 ($C3_{benzoic\ acid}$), 129.5 ($C4_{benzoic\ acid}$), 128.6 ($C5_{benzoic\ acid}$), 27.6 ($C2_{propionic\ acid}$), 8.9 ($C3_{propionic\ acid}$).

(viii) Benzoic acid and butyric acid (*from valerophenone*):
^{1}H NMR, δ: 11.4 (s, 1H, 1-$H_{benzoic\ acid}$), 10.2 (s, 1H, 1-$H_{butyric\ acid}$), 8.1 (д, 2H, 2-$H_{2,\ benzoic\ acid}$), 7.6 (t, 2H, 3-$H_{2,\ benzoic\ acid}$), 7.5 (t, 1H, 4-$H_{benzoic\ acid}$), 2.3 (t, 2H, 2-$H_{2,\ butyric\ acid}$), 1.7 (m, 2H, 3-$H_{2,\ butyric\ acid}$), 1.0 (t, 3H, 4-$H_{3,\ butyric\ acid}$).
^{13}C NMR, δ: 180.6 ($C1_{butyric\ acid}$), 172.4 ($C1_{benzoic\ acid}$), 133.8 ($C2_{benzoic\ acid}$), 130.2 ($C3_{benzoic\ acid}$), 129.5 ($C4_{benzoic\ acid}$), 128.5 ($C5_{benzoic\ acid}$), 36.1 ($C2_{butyric\ acid}$), 18.2 ($C3_{butyric\ acid}$), 13.6 ($C4_{butyric\ acid}$).

Results and discussion

Kinetic Results

Under pseudo–first-order conditions, the reactions showed a first-order dependence in [QDC], as seen from the constancy in the values of the pseudo–firstorder rate constant (k_1) over the range of QDC concentrations (Tables 1, 2). The reactions exhibited a firstorder dependence on the concentration of the substrate. In the range of acid concentrations (2.0–4.0 mol dm^{-3} H_2SO_4), the reactions showed a first-order dependence on the concentration of the acid. All these results are shown in Tables 1, 2. The acid catalysis was related to the structure of the oxidant, and at concentrations of acid larger than 0.05 M (range of acid concentrations in the present investigation was 0.50–1.50 M H_2SO_4 for cyclic ketones and 2.0–4.0 M $HClO_4$ for arylalkyl ketones), the dichromate ion was shown to be the predominant species [16]. The rate law could therefore be expressed as:

$$\text{Rate} = k\,[\text{substrate}]\,[\text{QDC}]\,[H^+]$$

Table 1 Rate data for the oxidation of cyclic ketones by QDC at 323 K[a]

[Cyclic ketones] × 10^2, M	[QDC] × 10^4, M	[H_2SO_4], M	$k_1 \times 10^4$, s^{-1}			
			Cyclopentanone	Cyclohexanone	Cycloheptanone[b]	Cyclooctanone[b]
10.0	10.0	1.0	0.70	3.34	0.51	2.06
50.0	10.0	1.0	3.51	16.8	2.61	10.4
75.0	10.0	1.0	5.24	25.1	–	–
100.0	10.0	1.0	7.1	33.4	–	–
10.0	7.5	1.0	0.71	3.30	0.52	2.08
10.0	5.0	1.0	0.68	3.33	0.50	2.03
10.0	2.5	1.0	0.69	3.31	0.53	2.09
10.0	10.0	1.50	1.05	5.01	0.76	3.12
10.0	10.0	0.75	0.53	2.49	0.38	1.53
10.0	10.0	0.50	0.34	1.68	0.25	1.05

[a][AcOH] = 20% (v/v).
[b]Sparingly soluble at concentrations higher than 0.5 M.

Table 2 Rate data for the oxidation of arylalkyl ketones[a] by QDC at 323 K[b]

[Substrate] × 10^2, M	[QDC] × 10^3, M	[$HClO_4$], M	$k_1 \times 10^4$, s^{-1}			
			1	2	3	4
1.0	1.0	2.0	0.92	0.56	0.48	0.41
2.5	1.0	2.0	2.3	1.4	1.2	1.1
5.0	1.0	2.0	4.6	2.8	2.4	2.1
7.5	1.0	2.0	6.4	3.9	3.6	3.3
10.0	1.0	2.0	9.3	5.5	4.9	4.3
20.0	1.0	2.0	19.0	11.0	9.8	8.5
1.0	0.75	2.0	0.93	0.57	0.49	0.40
1.0	0.50	2.0	0.94	0.59	0.48	0.38
1.0	0.25	2.0	0.97	0.56	0.49	0.40
1.0	0.10	2.0	0.96	0.58	0.47	0.41
1.0	1.0	2.5	1.15	0.71	0.61	0.54
1.0	1.0	3.0	1.38	0.85	0.73	0.65
1.0	1.0	3.5	1.70	0.98	0.85	0.77
1.0	1.0	4.0	1.83	1.12	0.96	0.88

[a]1: Acetophenone; 2: Propiophenone; 3: Butyrophenone; 4: Valcrophenone.
[b]Solvent = 20%; DMF; %; v/v

The effect of temperature was studied, and the activation parameters calculated are shown in Tables 3, 4. The negative values of $\Delta S^{\neq}$ provided support for the formation of a rigid activated complex which was strongly solvated.

Table 3 Effect of temperature and activation parameters for oxidation of cyclic ketones[a]

$T \pm 0.1$, K	$k_1 \times 10^4$, s^{-1}			
	Cyclopentanone	Cyclobexanone	Cycloheptanone	Cyclooctanone
313	0.35	1.71	0.25	1.06
318	0.50	2.50	0.36	1.25
323	0.70	3.34	0.51	2.06
328	1.03	4.51	0.72	2.51
333	1.41	6.7	1.03	4.15
$\Delta H^{\neq}$, kJ mol^{-1}	60 ± 2.1	45 ± 1.9	63 ± 2.3	54 ± 2.2
$\Delta S^{\neq}$, J mol^{-1} K^{-1}	–141 ± 3.8	–173 ± 4.1	–134 ± 3.6	–152 ± 3.3

[a][Cyclic ketones] = 0.1 M; [QDC] = 0.001 M; [H_2SO_4] = 1.0 M; [AcOH] = 20% (v/v).

Table 4 Temperature and activation parameters for oxidation of arylalkyl ketones[a, b]

$T \pm 0.1$, K	$k_1 \times 10^4$, s^{-1}			
	1	2	3	4
313	0.47	0.28	0.23	0.21
318	0.71	0.42	0.36	0.32
323	0.92	0.56	0.48	0.41
328	1.4	0.85	0.73	0.63
333	1.8	1.1	0.95	0.83
$\Delta H^{\neq}$, kJ mol^{-1}	42 ± 2.4	59 ± 2.8	65 ± 2.3	68 ± 2.9
$\Delta S^{\neq}$, J mol^{-1} K^{-1}	–186 ± 4.7	–137 ± 5.1	–112 ± 5.5	–107 ± 4.6

[a]1: Acetophenone; 2: Propiophenone; 3: Butyrophenone; 4: Valerophenone.

[b][Substrate] = 0.01 M; [QDC] = 0.001 M; [$HClO_4$] = 2.0 M; solvent = 20% DMF (%, v/v).

The effect of changes in the solvent composition (water–acetic acid and water–DMF) on the rate of oxidation was studied. The dielectric constants (D) of water–acetic acid mixtures and for water–DMF mixtures were calculated [17] from the D of the pure solvents (at 50°C, water = 69.9, acetic acid = 6.5, DMF = 37.6). It was observed that a decrease in the polarity of the medium (from 5% acetic acid to 20% acetic acid and from 0% DMF to 20% DMF) showed a decrease in the rate (Tables 5, 6). The magnitude of this effect suggested that, for the equilibrium $2HCrO_4^- \rightleftharpoons Cr_2O_7^{2-} + H_2O$, a decrease in D favored the dichromate form over the chromate form. Although the range of D used was not large, plots of log k_1 against $1/D$ were linear, with negative slopes, suggesting the possibility of an ion–dipole type of interaction [18].

Table 5 Effect of solvent on the rate of oxidation of cyclic ketones[a] at 323 K

H_2O/AcOH (%, v/v)	Dielectric Constant (D)	$k_1 \times 10^4$, s^{-1}			
		Cyclopentanone	Cyclohexanone	Cycloheptanone	Cyclooctanone
95 : 5	76.5	1.38	4.39	1.16	3.16
90 : 10	72.8	1.16	3.91	0.95	2.78
85 : 15	69.1	0.96	3.65	0.71	2.42
80 : 20	65.4	0.70	3.34	0.51	2.06

[a][Substrate] = 0.1 M; [QDC] = 0.001 M; [H_2SO_4] = 1.0 M

Table 6 Effect of solvent on the rate of oxidation of arylalkyl ketones[a, b] at 323 K

H_2O/DMF (%, v/v)	Dielectric Constant (D)	$k_1 \times 10^4$, s^{-1}			
		1	2	3	4
100 : 0	69.9	1.31	0.89	0.78	0.69
95 : 5	68.3	1.21	0.80	0.69	0.61
90 : 10	66.7	1.10	0.71	0.61	0.54
85 : 15	65.1	1.01	0.63	0.54	0.47
80 : 20	63.5	0.92	0.56	0.48	0.41

[a]1: Acetophenone; 2: Propiophenone; 3: Butyrophenone; 4: Valerophenone.

[b][Substrate] = 0.01 M; [QDC] = 0.001 M; [$HC10_4$] = 2.0 M.

Induced Polymerization

It was observed that there was no induced polymerization of acrylonitrile [19], ruling out the possibility of any free radicals being formed during the course of the reaction. Control experiments, performed in the absence of the substrate, did not show any appreciable change in [QDC].

Evidence for Enol Formation

Cyclic ketones

There was the possibility that the enol was an intermediate in the reaction. The formation of the enol was not rate-determining, since the rate of oxidation had a first-order dependence on [QDC], and the rate of enolization (bromination reaction) was more rapid (by a factor of ~20–25) than the rate of oxidation. A kinetic isotope effect was observed (k_H/k_D = 5.80) while comparing the rates of oxidation of cyclohex anone and cyclohexanone–d_4, respectively. If the reaction involved the enol intermediate, then the kinetic isotope effect observed (k_H/k_D = 5.80) has to be explained. The presence of the α-deuterium would result in the rate of formation of the enol being decreased, while the conversion of the enol to the ketone (the reverse reaction) would proceed at a normal rate. The steady-state concentration of the enol would thus be reduced by a factor corresponding to the isotope effect for enolization. Any subsequent reaction dependent on the concentration of the enol would accordingly be reduced in rate.

Arylalkyl ketones

In oxidation reactions, ketones could react either directly or through the enol form. Oxidation rates faster than the rates of enolization have been observed with eerie [20, 21], manganic [21] and cobaltic salts [21,

22] as oxidants, indicating that the ketones reacted directly. All of these oxidants underwent one-electron reduction, and the reactions were through a free radical mechanism [20–22]. In the oxidations by manganic pyrophosphate [23]; thallic, mercuric, and permanganate salts [24]; and potassium bro- mate [11], the enol formation was rate-determining and the reactions were zero order in the oxidant (rates of oxidation and enolization being equal). An unambigu- ous indication of the form in which the ketone reacted could be obtained only by comparison of the two rates (of oxidation and enolization). In the present investigation, if the step involving enolization were to be rate- determining, then the rate of oxidation would have been independent of [QDC].

However, the kinetic data (Tables 1, 2) showed a first-order dependence on [QDC], and the rate of enolization (measured by the bromination method) was greater than the rate of oxidation by a factor of ~12–15. This suggested that the step involving the formation of the enol (from the ketone) was a fast step and hence was not the rate-determining step of the reaction. Moreover, in the step involving the formation of the enol, there was a rapid change in the state of hybridization of the ketone from the sp^2 to the sp^3 state at the site of attack. The next step involving the reaction of the enol form (of the substrate) with the oxidant would be the crucial and rate-determining step of the reaction. This mechanistic pathway finds support from earlier investigations wherein it was shown that ketones were oxidized via the enol form [8–11].

Structural Influences

Cyclic ketones (ring size)

The rate data in Table 1shows the order of reactivity for the cyclic ketones:

cyclohexanone > cyclooctanone > cyclopentanone > cycloheptanone.

This would become more relevant and meaningful only when conformational aspects were taken into consideration. In its chair form, cyclohexanone would owe its unique stability to the fact that each of its energy components would be a minimum. A more favored model would be a form with only four carbon atoms planar, which would be similar to the half-chair cyclohexene in shape [25]. This form would be the direct intermediate conformation between the chair form and the twist-boat form, all of C_{2v} symmetry. The interconversion of chair to twist-boat takes place by a rotation of one bond around the 2-fold axis. Since this is the most economical route for boat–chair conversion, it is probably also the most economical pathway for deformations of the six-membered cycloalkanone. Hence, the reactivity of cyclohexanone would be the highest among the cycloalkanones.

Cyclooctanone has C_{2v} symmetry, resulting in a particular type of deformed crown structure [26, 27]. There appear to be three different kinds of axial positions and three different kinds of equatorial positions, indicating that cyclooctanone is a mixture of six conformations (some possibly in negligible amounts). In cyclooctanone, the oxygen is compressed by the hydrogen atoms at C1 and C5 and there is no significant relief of this compression when cyclooctanone is subjected to oxidation. Hence, the rate of oxidation of cyclooctanone would be slower than that for cyclohexanone.

The lower reactivity of cyclopentanone was due to the existence of cyclopentanone in the half-chair form (stable conformation) having greater symmetry [28].

For cycloheptanone, there were two forms that could be interconverted through major deformations of bond angles from tetrahedral. These two plane-symmetrical forms were the chair form and the boat form. However, both forms would be flexible with respect to their bond angles and may undergo pseudorotation. The chair form has a H–H repulsion across the axial C3-positions, which may be relieved by pseudorotation. In the boat form, the half-cycle position provided minimum repulsion energy. This form has a 2-fold symmetry axis, called the twist–chair conformation [29]. This would be the stable form and would account for the extremely low reactivity of cycloheptanonewhen subjected to oxidation.

Supporting arguments for the observed order of reactivity for cyclic ketones [$C_6 > C_8 > C_5 > C_7$ (ring size)] could be based on the following considerations:

(a) I-strain in these rings. The concept of I-strain has been invoked to explain the relative ease with which a change in the bond hybridization (sp^2- sp^3) takes place in these ring compounds [30]. The change may refer to the formation of a transition state or of a product leading to a kinetic effect or a thermodynamic effect, respectively. In the rate-determining step of the reaction, one of the ring-carbon atoms changes from the sp^2 to the sp^3 state of hybridization. The relative ease of such a change in the state of hybridization is inthe order (ring size): $ë_6 > ë_8 > ë_5 > ë_7$ [31].

(b) Cyclohexanone is essentially free of strain. The strain due to eclipsing of the carbonyl oxygen by the equatorial hydrogen atoms at C2 and C6 appears to be relieved when the hybridization of the carbonyl oxygenis changed from sp^2 to the sp^3.

(c) The higher reactivity of cyclohexanone is due to the terminal hydrogen of the nearly strainless puckered $(CH_2)_4$ residue, fulfilling the stereochemical requirement for hyperconjugation with the cyclic C=C groups better than the terminal hydrogen of the nearly flat $(CH_2)_3$ residue in cyclopentanone does [32]. This also explains the higher enol content for cyclohexanone, as compared with the other medium-ring ketones.

(d) The higher reactivity of cyclohexanone is a natural consequence of the higher enolic content. The enolization of ketones consists of two steps:

(i) equilibrium protonation of the carbonyl group; and

(ii) deprotonation of the α-carbon of the conjugate acid.

These two steps affect the rate of enolization.

(e) The enolization rate constants for cyclic ketones have been reported [33]. The higher enolization constant of cyclohexanone is probably the most important factor contributing towards its greater reactivity, com- pared to that of cycloheptanone. In the step involving the formation of the enol, there is a change in the state of hybridization of the ketone from sp^2 to sp^3 at the site of attack. The

conversion from sp^2 to sp^3 is most favored for a six-membered ring, and least favored for a seven-membered ring [34].

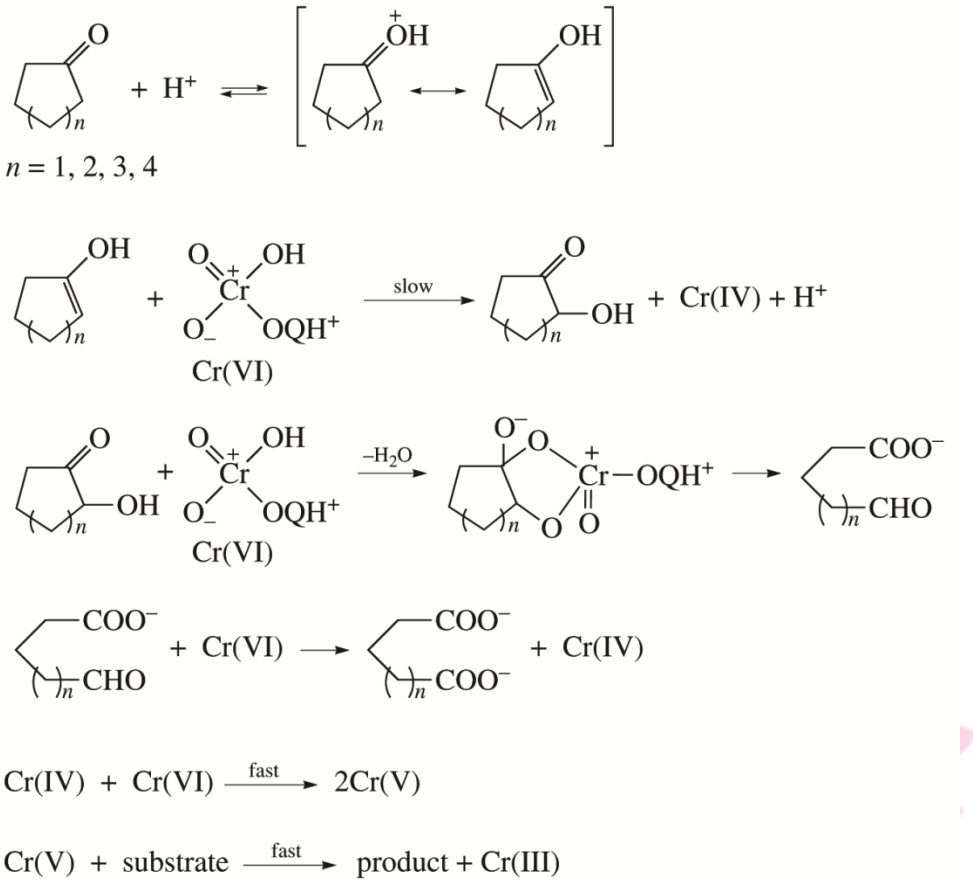
Arylalkyl ketones

The order of reactivity was in accordance with the structural changes acetophenone > propiophenone > butyrophenone > valerophenone (Table 2). Owing to the inductive effect, the presence of the methyl group in propiophenone enhanced the electron density at the carbon atom adjacent to the carbonyl group. The ease of deprotonation from this carbon atom in propiophenone would decrease as compared to that in acetophenone. The +I effect becomes more pronounced with respect to butyrophenone and valerophenone, due to the presence of the C_2H_5 and C_3H_7 groups respectively, resulting in a further decrease in the rate of oxidation. The tendency of alkyl groups to decrease the electron density on the α-carbon would check the loss of the proton attached to the same α-carbon atom. Hence, an increase in the +I effect of the alkyl groups would result in a decrease in the rate of oxidation (Table 2).

Mechanism

Cyclic ketones

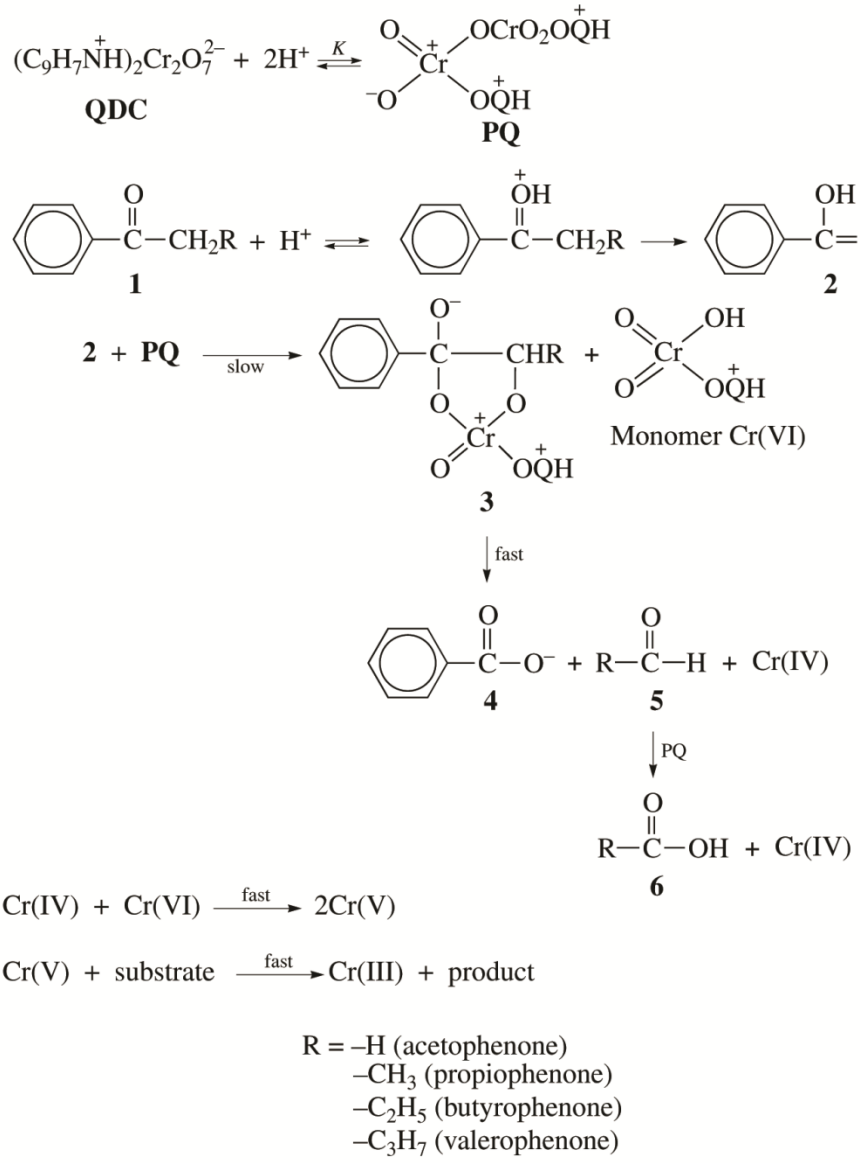
The rate–determining step involved an attack of the oxidant on the enol form of the substrate (Scheme 1). The large negative entropies of activation were consistent with the formation of a cyclic intermediate in a bimolecular reaction. Coordination of the chromium through the –OH group of the oxidant would facilitate the formation of the chromate ester. If the chromium were to be coordinated through the oxygen, then the process of electron transfer could take place through the carbon–oxygen–chromium bond. This would not only enable the formation of the chromate ester, but would also enhance the ease of conversion to the product. This electrocyclic mechanism involved six electrons; being a Hückel–type system (4n + 2), this was an allowed process [35, 36]. This mechanism was consistent with the fact that the oxidation reactions were acid-catalyzed. Protonation of the oxidant would make it more amenable towards nucleophilic attack by the enol form of the substrate on the electron-deficient chromium of the oxidant.



Scheme 1

Arylalkyl ketones

There existed the possibility of equally equivalent accessibility of the *–ene* and the hydroxyl group of the enol to the reaction center. This conformational insensitivity could be attributed to the cyclic nature of the transition state. If the reaction inter- mediate was visualized as having a cyclic structure, then this would explain all the features of the oxidation reaction. Further, the small variation in the reaction rate for the oxidation reactions (Table 2) could be recon- ciled with the ester mechanism, since cyclic chromate ester formation was likely to be little influenced by structural changes [37]. The mechanistic pathway has been shown in Scheme 2: Arylalkyl ketones **1** were converted to the enol **2**, which reacted with **PQ**, in the rate-determining step, giving the cyclic chromate ester **3**. The decomposition of the cyclic chromate ester was through the carbon–oxygen–chromium bond of **3**, giving the open structures **4** (carboxylic acid) and **5** (aldehyde). On oxidation with another mole of **PQ**, **5** was converted to the corresponding carboxylic acid **6**, along with the formation of the Cr(IV) species.



Scheme 2

The conversion of Cr(IV) to Cr(III) has been established as proceeding via a disproportionation reaction,with favorable standard potentials for the Cr(VI)–Cr(V)and Cr(V)–Cr(III) couples [38, 39].

The kinetic data and the nature of the products obtained clearly showed that the oxidation of ketones (cyclic and arylalkyl) by QDC was through the enol form of the substrate, which led to the cleavage of the carbon–carbon bond, yielding carboxylic acids. While highlighting the importance of QDC as an oxidant, this study emphasized the efficiency of this oxidative cleavage route for the regioselective synthesis of carboxylic acids.

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