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Conformational and steric effects on the oxidation of some cyclic ketones by pyridinium fluorochromate

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The kinetics of oxidation of cyclohexanone, cyclopentanone, cycloheptanone, cyclooctanone and various alpha substituted cyclohexanones by pyridinium fluorochromate(PFC) has been followed under pseudo-first order conditions in aqueous acetic acid medium in the presence of $HClO_4$. The reaction is first order both in oxidant and substrate. The rate increases linearly with increasing [$HClO_4$]. The salt and solvent influences together indicate the reaction to be an ion-dipole type. The stoichiometry between the substrate and oxidant is 1:2 and the product of oxidation is 1,2-diketone. The relative reactivities of various cyclic ketones have been rationalised on the basis of conformational differences and steric factors.

The chemistry of alicyclic ketones is of interest because of the stereochemical properties inherent in their ring systems. The literature survey has revealed that the kinetics of oxidation of cycloalkanones by a variety of oxidants both in acid and alkaline medium have been carried out. Oxidation by hexacyanoferrate(III)[1], vanadium(V)[2], cerium(IV)[3], phenyl iodosoacetate[4], potassium bromate[5], *N*-bromosaccharin[6] and chloramine-B[7] are to quote some of them. Although oxidation of cycloalkanones has received considerable attention, the reports on the oxidation of substituted cyclohexanones is found to be scarce. Further, chromic acid oxidation of cyclic ketones generally leads to C-C bond cleavage and the interest lies in finding whether pyridinium fluorochromate (PFC), being mild in its action, can effect ring scission or not. Hence, the present investigation is initiated with a view to understanding the interrelationship of conformation, reactivity and mechanism in the oxidation of these substrates by PFC.

Materials and Methods

All the chemicals used were of analytical grade. Triply-distilled conductivity water and purified acetic acid were used. The susbtrates, viz., cyclohexanone, cyclopentanone, cyclohepatanone and cyclooctanone were purified through their bisulphite addition compounds followed by distillation. Substituted cyclohexanones were prepared as described earlier[8]. PFC was obtained by the reported method[9] and its purity was checked by UV spectral analysis and by iodometry. The acidity of all the solutions was adjusted by using $HClO_4$ and the ionic strength by $NaClO_4$. The kinetic studies were carried out in 50%(v/v) aqueous acetic acid under pseudo-first order conditions by keeping the [substrate] and [acid] always in excess over that of [PFC]. The reactions were followed at constant temperatures (±0.1°C), by determining unreacted [PFC] at different time intervals spectrophotometrically at 350 nm. The pseudo-first order rate constants, k_1, computed from the linear (r>0.990, s < 0.020) plots of log absorbance against time by least squares method, were reproducible within ±3%. The error quoted in k value is the 95% confidence limit of student's 't' test.

Stoichiometry and product analysis

Different ratios of [PFC] to [substrate] were mixed in the presence of $HClO_4$ at room temperature. The estimation of unchanged PFC after 24 hr showed that one mol of ketone consumed 2 mol of PFC in accordance with Equation 1.

$$C_6H_{10}O+2\ CrO_3FPyH \rightarrow C_6H_8O_2+2CrO_2FPyH+H_2O \quad ...(1)$$

The reaction mixture was analysed to identify the product after keeping it for two days for completion. After the evaporation of the solvent under reduced pressure, the residue was extracted with dichloromethane. It was then washed with H_2O and dried over anhydrous sodium sulphate. The oily liquid obtained after the evaporation of dichloromethane was treated with hydroxylamine hydrochloride, sodium acetate and Ni(II). Development of pink colour confirmed the product to be 1,2-diketone[10]. The product was further characterised by TLC and IR spectra.

Results and Discussion

Oxidation of all the nine cyclic ketones studied exhibited similar kinetic features and hence the results of cyclohexanone are presented here as a typical one. In control experiments without the ketone the concentration of PFC was found to be constant.

At fixed [acid] and with [substrate] in excess the plots of log absorbance versus time are linear (r >0.997, s<0.014) indicating first order dependence on [PFC]. But the first order rate constants, k_1, are found to decrease with the increase in gross [PFC] (Table I). Similar observations have been made earlier in different oxidation studies[11-13] including the oxidation by PFC[14].

The pseudo-first order rate constants are found to increase with the increase in [substrate]. Plot of log k_1 versus log [substrate] is linear (r=0.999, s=0.003) with a unit slope. Further, the second order rate constant, $k_2=k_1$/[substrate], is found to be almost constant confirming first order dependence on [substrate] (Table I).

The reactions are acid-catalysed and a good correlation (r=0.997, s=0.019) has been observed when log k_1 is plotted against log [$HClO_4$] with a unit slope indicating first order dependence with respect to [$HClO_4$]. The pronounced increase in the oxidation rate with acidity (Table I) suggests the involvement of protonated Cr(VI) species in the rate-controlling step. Participation of such species has been observed in earlier reports[15-17]. Being a better electrophile, the protonated form of PFC can function as a stronger oxidant and this accounts for acid-catalysis.

Table I—Effect of reactant concentrations on the oxidation of cyclohexanone by PFC at 308 K {AcOH : H_2O = 50:50(v/v)}

[PFC]×10^3 (mol dm^{-3})	[Substrate]×10^2 (mol dm^{-3})	[$HClO_4$] (mol dm^{-3})	k_1×10^4 (s^{-1})
4.0	5.0	1.50	4.20±0.29
5.0	5.0	1.50	3.74±0.11
5.5	5.0	1.50	3.50±0.02
7.0	5.0	1.50	3.38±0.09
8.5	5.0	1.50	3.36±0.15
7.0	1.0	1.50	0.696±0.02
7.0	2.5	1.50	1.76±0.06
7.0	5.0	1.50	3.38±0.09
7.0	7.5	1.50	5.33±0.09
7.0	10.0	1.50	7.05±0.17
7.0	5.0	0.50	0.84±0.02
7.0	5.0	1.00	1.94±0.05
7.0	5.0	1.25	2.58±0.14
7.0	5.0	1.50	3.38±0.09
7.0	5.0	2.00	4.23±0.12

Table II—Influence of ionic strength and solvent polarity on the rate of oxidation of cyclohexanone by PFC at 308 K {[Substrate] = 5.0 ×10^{-2} mol dm^{-3}; [PFC] = 7.0×10^{-4} mol dm^{-3}; [$HClO_4$]=1.50 mol dm^{-3}}

Acetic acid (%)	μ (mol dm^{-3})	k_1 × 10^4 (s^{-1})
30	2.00	1.99±0.12
40	2.00	2.30±0.07
50	2.00	3.33±0.07
60	2.00	5.71±0.26
70	2.00	20.9±0.45
50	1.50	2.70±0.04
50	2.00	3.33±0.07
50	2.25	3.73±0.06
50	2.50	4.38±0.11
50	3.00	5.01±0.19

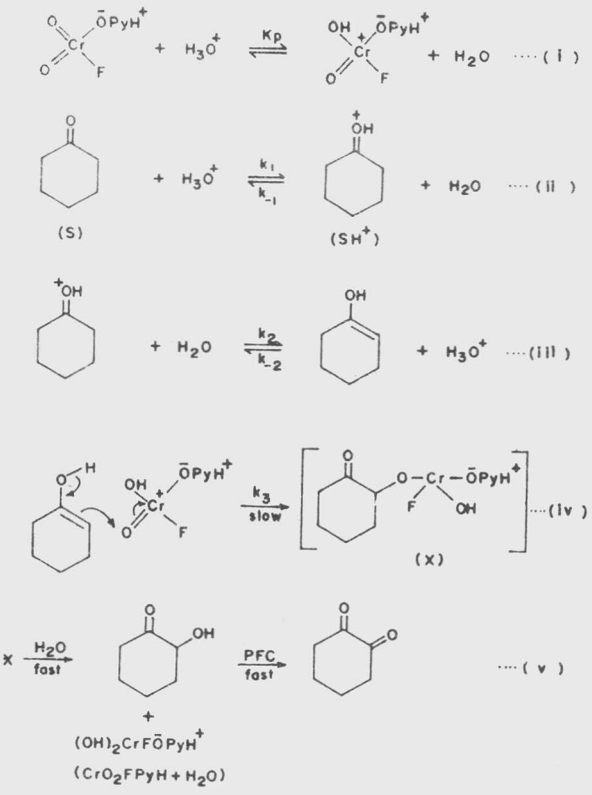
The sensitivity of the reaction to solvent polarity was studied by changing the composition of acetic acid in the medium and the results are recorded in Table II. An increase in the proportion of acetic acid in the solvent mixture increases the rate of oxidation enormously. A plot of log k_1 against the inverse of dielectric constant of the medium is linear (r=0.998, s=0.027) with a positive slope implying the reactive species in acid medium to be a positively charged one[18] and this provides convinving evidence that PFC is protonated.

It is obvious from Table II that there is a small but steady increase in the rate with the increase in

ionic strength of the medium. A good correlation is observed between log k_1 and μ (r=0.993, s=0.014) indicating the participation of a neutral molecule and an ion in the rate-determining step of the reaction[19].

Oxidation of various cyclic ketones has been carried out at four different temperatures. The second order rate constants and various activation parameters are presented in Table III. The precision of $\Delta H^{\#}$ and $\Delta S^{\#}$ was calculated by the method of Petersen *et al*[20]. The observed negative $\Delta S^{\#}$ value reflects the loss of entropy incurred in bringing two reactant molecules to form a single activated complex. The isokinetic temperature, as obtained (408 K) from the slope of Exner's[21] linear plot (r=0.997, s=0.042) of log k_2 (at 308 K) versus log k_2 (at 298 K), lies above the experimental temperature. This implies that these oxidations are enthalpy controlled. The existence of the isokinetic temperature suggests a common mechanism and similar transition states for all the nine oxidations.

Addition of reaction mixture to acrylonitrile in an inert atmosphere did not induce polymerisation of the latter showing the absence of free radical intermediates.



Scheme I

Mechanism

In accordance with the above kinetic and nonkinetic results, the various mechanistic steps are outlined in Scheme I. In the oxidation reaction a ketone may react directly or through its enol form. PFC, being an efficient two-electron oxidant[22] prefers to attack the enol form. The formation of enol cannot be rate-determining since the rate depends on [PFC] and also the rate of bromination was found to be faster than the rate of oxidation. Hence, the rate-determining step is assumed to involve a two-electron transfer from the enol to PFC leading to the formation of an α-keto ester in chromic acid oxidations is well known[11]. The first stage oxidation product, α-

Table III — Rate constants at different temperatures and activation parameters on the oxidation of cyclic ketones by PFC {[Substrate]=5.0×10^{-2} mol dm^{-3}; [PFC] = 7.0 × 10^{-4} mol dm^{-3}; [$HClO_4$] = 1.50 mol dm^{-3} ; ACOH: H_2O = 50: 50 (v/v)}

Substrate	$k_2 \times 10^3$ (mol dm^{-3}s^{-1})					$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$	$\Delta G^{\ddagger}$
	288K	298K	308K	318K	328K	(kJ mol^{-1})	(JK^{-1} mol^{-})	(kJ mol^{-1})
Cyclopentanone	–	0.538±0.12	1.35±0.05	2.82±0.07	6.14±0.23	62.8±4.3	96.2±15	92.4
Cyclohexanone	–	3.42±0.0	6.76±0.18	12.5±0.56	25.9±1.04	51.8±1.5	119±5.3	88.3
Cycloheptanone	–	1.75±0.08	4.64±0.19	8.76±0.38	15.2±0.52	55.4±2.2	110±7.8	89.3
Cyclooctanone	–	1.79±0.08	4.74±0.24	10.4±0.30	19.2±0.46	61.8±2.0	89.1±7.0	89.2
2-Methylcyclo-hexanone	6.38±0.0	13.4±0.12	28.3±1.46			52.5±0.6	104±2.2	84.6
2-Ethylcyclo-hexanone		7.80±0.44	15.5±0.78	25.9±0.60	42.7±0.96	43.1±2.0	140±7.2	86.2
2-Isopropyl-5-methylcyclo-hexanone		2.08±0.11	4.64±0.09	9.90±0.34	19.3±1.02	58.0±2.2	102±7.6	89.3
2-Benzylcyclo-hexanone	29.1±2.5	53.8±7.5	79.9±10			34.9±8.6	153±31	82.0
2-Chlorocyclo-hexanone		8.60±0.44	16.0±0.90	33.1±0.58	50.3±2.28	46.5±2.3	129±8.1	86.1

hydroxyketone could not be isolated as it is readily oxidised to 1,2-diketone. With step IV (Scheme I) as the rate-determining step, the rate of the reaction is given by Eqn. (2)

$$\text{rate} = -d[\text{PFC}]=k_3[\text{enol}][\text{PFCH}^+] \quad \ldots(2)$$

Aplying steady-state treatment to $[SH^+]$, the protonated ketone, and assuming $k_1 >> k_2$ it can be shown that

$$[\text{enol}] = \frac{k_1 k_2 [\text{S}][\text{H}_3\text{O}^+]}{(k_{-1} + k_2)(k_2[\text{H}_3\text{O}^+] + k_3[\text{PFCH}^+])} \quad \ldots (3)$$

Inserting this in Eq. (2) we get,

$$[\text{rate}] = \frac{k_1 k_2 k_3 [\text{S}][\text{PFCH}^+][\text{H}_3\text{O}^+]}{(k_{-1} + k_2)(k_2[\text{H}_3\text{O}^+] + k_3[\text{PFCH}^+])} \quad \ldots (4)$$

$Rs[PFCH^+]$ can be neglected.

Under the present experimental conditions, since $[H_3O^+] >> [PFCH]$, $K_3[PFCH^+]$ can be neglected in comparison[20] $K_2[H^+{}_3O]$ and rate becomes.

$$\text{rate} = \frac{k_1 k_2 k_3 [\text{S}][\text{PFCH}^+]}{(k_1 + k_2)k_2} \quad \ldots (5)$$

Taking advantage of the preliminary equilibrium protonation of PRC shown in step(i) (Scheme I), the final rate of revision can be written as,

$$\text{rate} = k_2[\text{S}][\text{PFC}][\text{H}_3\text{O}^+] \quad \ldots (6)$$

The rate expression (Eq. 6) accounts for the experimental observations.

Effect of ring size

It is obvious from Table III that the rate constants for the oxidation varies in the order: cyclohexanone > cyclooctanone~cycloheptanone > cyclopentanone. The possible explanation could be based on I-strain in these rings. The concept of I-strain was invoked[23] to explain the relative ease with which a change in bond hybridisation, sp^2 to sp^3 or sp^3 to sp^2 takes place in ring compounds. The change may refer to the formation of a transition state or of a product leading to a kinetic effect or thermodynamic effect, respectively. In the rate-controlling step of the reaction (Step IV, Scheme I) one of the ring carbon atoms changes from sp^2 to sp^3 hybridisation. The relative ease of such change in hybridisation is in the order[24]: cyclohexanone > cyclooctanone~cycloheptanone > cyclopentanone. An extract reverse order of reactivity reported in the oxidation of cycloalkanols[25], wherein the transition from sp^3 to sp^2 is to be regarded, is in support of this view.

Effect of substituents

An analysis of rate data presented in Table III shows that the order of reactivity among the substituted cyclohexanones is 2-benzyl > 2-methyl >2-chloro > 2-ethyl > H > 2-isopropyl. The rate differences may be explained based on steric factors and conformational effects in the ground(1) and transition states(2). An examination of Dreiding-stereo models has revealed the possibility of non-bonded steric interactions between enolic O-H and the vicinal alkyl group in the ground state. The magnitude of such interactions are expected to increase in the order methyl, ethyl, isopropyl and benzyl: A remarkable increase in the oxidation of 2-benzylcyclohexanone may be due to greater steric relief experienced in going to the relatively strain-free transition state. An equatorial alkyl group (except methyl) in the 2-position is nearly eclipsed[26] with the carbonyl oxygen thereby dstabilising the transition state and lowering the rate of oxidation. As expected the rate retardation due to this destabilisation is greater for isopropyl than for ethyl and hence the rate goes even below that of unsubstituted cyclohexanone when the substituent is isopropyl. The enhanced reactivity of 2-chlorocyclohexanone may be ascribed to the electron-withdrawing nature of chlorine facilitating the release of enolic proton in the rate-determining step of the oxidation process.

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