Kinetics and Oxidation of 3,5-Dimethyl-2,6-diaryl piperidin-4-one Oximes by Pyridinium Chlorochromate

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Kinetics of oxidation of 3,5-dimethyl-2,6-diaryl piperidin-4-one oximes by pyridinium chlorochromate have been studied in aqueous acetic acid medium. The oxidation is first order each in [oxidant] and [substrate]. The reactions are acid catalyzed. The effect of ionic strength on the reaction rate is negligible. The reaction rates are accelerated by increasing the dielectric strength of the medium indicating a polar mechanism. The reactions are followed at four different temperatures and the activation parameters computed. Based on the results obtained a plausible mechanism is proposed. The reactivity sequence is: *For para* substituted aryl compounds = H > 4-Cl > 4-Me > 4-OMe; For *ortho* substituted aryl compounds = H > 2-Me > 2-OMe > 2-Cl.

Key Words: Kinetics, Oxidation, Oximes, Pyridinium chlorochromate.

INTRODUCTION

Many valuable natural products with carbonyl groups are crystallized out only in the form of oximes and semicarbazones from their biological sources[1]. Oxidative hydrolysis of oximes and semicarbazones result in better yield of the corresponding ketones than acid hydrolysis. Metal ion oxidants are the reagents of choice for the regeneration of carbonyl compounds from the respective oximes and semicarbazones[2-7]. Oximes have been converted to the corresponding aldehydes or ketones by treatment with reagents like thallium(III)[8], manganese(IV)[3], 1-chlorobenzotriazole[9], peroxomono-sulphate[10], acid dichromate[11], PFC[12], NBSA[13], NBS[14] and QDC[15]. Among the above mentioned metal ion oxidants, chromium compounds play the most important role. Pyridinium chlorochromate (PCC) is found to oxidize a wide variety of compounds with high efficiency. From the literature survey it is found out that the pyridinium chlorochromate oxidation of entitled oximes have not been studied. Hence in the present paper we report the kinetics of oxidation of some 3,5-dimethyl- 2,6-diaryl piperidin-4-one oximes.

EXPERIMENTAL

Pyridinium chlorochromate (PCC) a complex of chromium trioxide and hydrochloric acid is prepared in the laboratory by the method cited in the literature[16] and its purity was checked by iodometric method. The oximes were prepared by the standard procedures[17,18]. Acetic acid used for kinetic runs was thrice distilled by adopting the usual procedures[19]. All the chemicals used were of analytical grade.

Kinetic procedure: The measurements were carried out in 60 % (v/v) aqueous acetic acid medium at four different temperatures keeping the concentration of the substrate in considerable excess over that of pyridinium chlorochromate (PCC). The ionic strength of the medium was maintained at 0.021 mol dm^{-3} by using Na_2SO_4 and sulphuric acid. The pseudo first order rate was followed by monitoring the decrease in absorption of pyridinium chlorochromate at 355 nm employing spectrophotometer. The pseudo first order rate constant k_{obs} was evaluated from the linear least square plots of log [PCC] *vs.* time and were found to be reproducible within ± 3 %. The reactions were carried out in the temperature range 278 to 298 K.

Test for free radical intermediates: No polymer forma-tion was obtained when a freshly distilled acrylonitrile mono-mer was added to a deaerated reaction mixture indicating the absence of free radical intermediate. The absence of influence of atmospheric oxygen on the reaction rate also suggests a non-radical reaction pathway.

Stoichiometry and product analysis: A known excess of pyridinium chlorochromate was allowed to react with a known concentration of corresponding oxime in 60 % aqueous acetic acid medium. Estimation of unreacted oxidant from the reaction mixture after the completion of the reaction showed that the stoichiometry of the reaction is 1:1. The reaction mixture was also analyzed for the products by qualitative tests. The

product was detected to be the corresponding ketone which was further confirmed by TLC experiments.

RESULTS AND DISCUSSION

Order with respect to oxime: The dependence of the rates of reaction on substrate concentration was studied by varying [oxime] in the range 0.5-1.5×10^{-3} mol dm^{-3} and fixed concentrations of the other reactants. The plot of log [PCC] *vs.* time (min) at different initial concentrations of oximes were linear and the value of k_{obs} (s^{-1}) evaluated from slopes were found to be dependent on the initial concentrations of the substrate. The plot of log k_{obs} *vs.* log [oxime] was linear with unit slope showing a first order dependence on [oxime]. The values of k_{obs} (s^{-1}) plotted against [substrate] gave straight lines passing through the origin, proving first order dependence on [oxime] (Fig. 1). From the slopes of the above plots, the second order rate constants k_2 (dm^3 mol^{-1} s^{-1}) were evaluated.
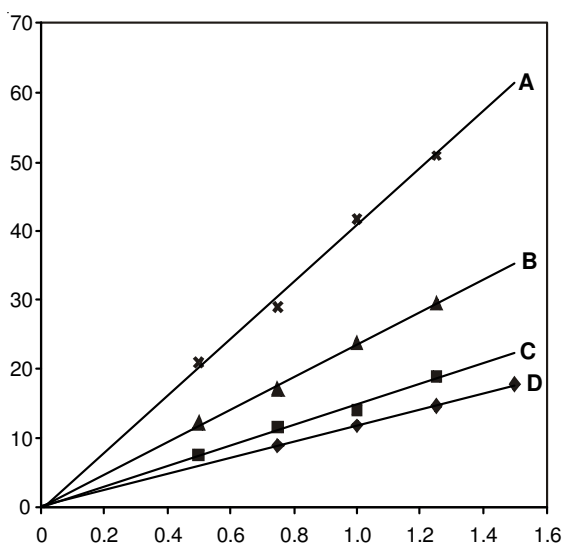

Fig. 1. $k_1 \times 10^4$ mol dm^{-3} (y-axis) *vs.* [substrate] $\times 10^2$ mol dm^{-3} (x-axis) Evaluation of k_2 at 293 K A-3,5-diMe-2-Cl PPO B-3,5-diMe-2-anisyl PPO C-3,5-diMe-4-Anisyl PPO D-3,5-diMe-2-Tolyl PPO

Order with respect to pyridinium chlorochromate: The concentration of pyridinium chlorochromate was varied in the range from 2.5-12.5×10^{-4} mol dm^{-3}. The fact that the plots of log [PCC] *vs.* time (min) were straight lines indicates that the reaction is first order in pyridinium chlorochromate. However the pseudo first order rate constants were found to decrease with increase in concentration of pyridinium chlorochromate (Table-1). Similar observations have been reported earlier in the oxidation studies involving other Cr^{6+} oxidants[20,21].

Effect of [H$^+$]: The acidity of the medium was varied from 1.0-4.0×10^{-3} mol dm^{-3} to investigate the effect of acid on the reaction rate at constant [PCC], [oxime] and ionic strength (0.021 mol dm^{-3}). The oxidation reactions were found to be acid catalyzed. The plot of log k_{obs} *vs.* log [H$^+$] were linear and the slope indicates fractional order with respect to [H$^+$].

Influence of ionic strength: The influence of ionic strength on the rate of reactions were determined by performing the reactions at different ionic strengths of the medium and maintaining [H$^+$] constant. The influence of ionic strength on the rates of oxidation was negligible indicating the interaction of an ion and a dipole in the rate determining step[22].

Dependence of solvent polarity: The effect of dielectric constant on the reaction rate was examined by varying the percentage of acetic acid in the range 40-70 % (v/v). The reaction rates were found to decrease with decreasing dielectric constant of the medium. This trend reveals that there is a charge development in the transition state involving a more polar activated complex than the reactants.

Rate and activation parameters: From the observed kinetic data, the second order rate constants were found to increase with increase in temperature. The plots log k_2 *vs.* 1/T were linear indicating that the Arrhenius law is being obeyed. The thermodynamic parameters E_a (kJ mol^{-1}), $G^{\neq}$ (kJ mol^{-1}) and $S^{\neq}$ (JK^{-1} mol^{-1}) have been computed and tabulated (Table-2).

Mechanism: In the light of all the experimental results obtained in the present investigation and the evidences from

TABLE-1
RATE DATA FOR THE OXIDATION OF 3,5-DIMETHYL-2,6-*BIS*(2-CHLOROPHENYL)PIPERIDIN-4-ONE
OXIME BY PYRIDINIUM CHLOROCHROMATE

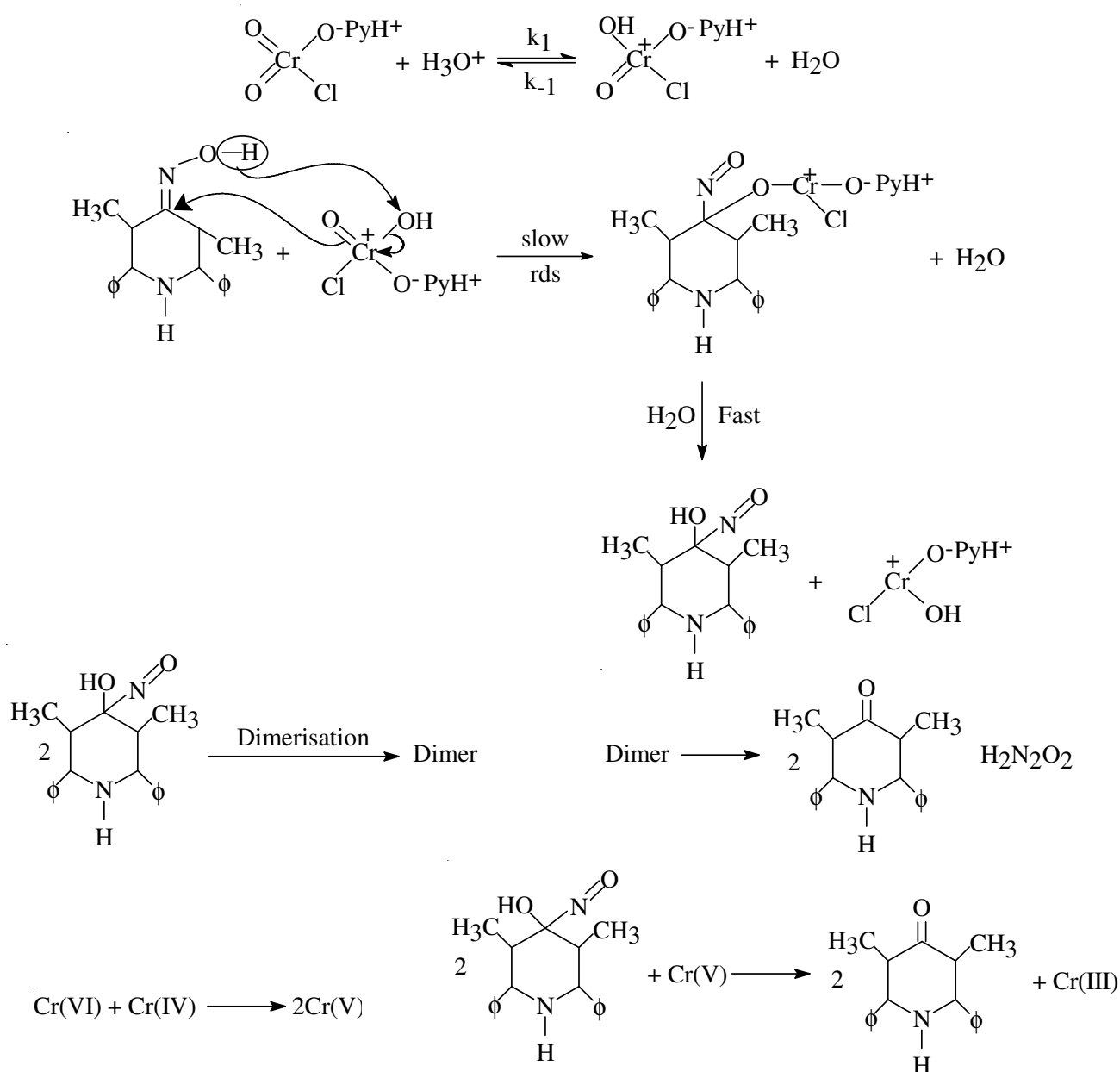| Pyridinium chlorochromate $\times 10^{-4}$ (mol dm^{-3})	3,5-diMe-2-Cl PPO $\times 10^{-2}$ (mol dm^{-3})	[H$_2$SO$_4$] $\times 10^{-3}$ (mol dm^{-3})	μ (mol dm^{-3})	AcOH:H$_2$O	$k_1 \times 10^{-4}$ (s^{-1})
2.5	1.00	2.0	0.021	60:40	39.22
5.0	1.00	2.0	0.021	60:40	24.88
7.5	1.00	2.0	0.021	60:40	11.84*
10.0	1.00	2.0	0.021	60:40	7.76
7.5	0.75	2.0	0.021	60:40	9.00
7.5	1.25	2.0	0.021	60:40	14.62
7.5	1.50	2.0	0.021	60:40	17.80
7.5	1.00	1.0	0.021	60:40	9.08
7.5	1.00	3.0	0.021	60:40	14.31
7.5	1.00	4.0	0.021	60:40	17.94
7.5	1.00	2.0	0.018	60:40	12.33
7.5	1.00	2.0	0.024	60:40	11.41
7.5	1.00	2.0	0.027	60:40	10.96
7.5	1.00	2.0	0.021	40:60	72.99
7.5	1.00	2.0	0.021	50:50	58.75
7.5	1.00	2.0	0.021	70:30	9.00

*at 283 K, 6.02, at 288 K 8.78, at 298 K 19.02.

TABLE-2
RATE CONSTANTS AND ACTIVATION PARAMETERS OF THE OXIDATION OF OXIMES

Substrate	--- 278 K	---k_2 283 K	$\times 10^2$ 288 K	dm^3 293 K	mol^{-1} 298 K	s^{-1} 303 K	------ 308 K	E_a KJ/mol	$\Delta H^{\neq}$ KJ/mol	$\Delta S^{\neq}$ J/K/mol	$\Delta G^{\neq}$ KJ/mol
3,5-diMe PPO	22.10	38.30	50.20	64.10	--	--	--	46.91	44.47	-96.70	72.81
3,5-dime-2-Cl PPO	--	6.02	8.78	11.67	19.02	--	--	52.91	50.48	-90.26	76.92
3,5-dime-4-Cl PPO	30.24	35.67	41.38	46.65	--	--	--	19.58	17.14	-192.64	73.58
3,5-diMe-2-Anisyl PPO	--	5.36	8.42	10.42	18.64	--	--	53.15	50.71	-88.09	76.52
3,5-diMe-4-anisyl PPO	--	19.10	20.95	23.55	33.44	--	--	24.84	22.41	-180.31	75.24
3,5-diMe-2-tolyl PPO	8.41	12.84	17.53	41.60	--	--	--	69.88	67.44	-21.88	73.86
3,5-diMe-4-Tolyl PPO	--	29.24	37.43	43.63	52.25	--	--	26.54	24.10	-169.43	73.75

the other investigations involving the oxidative hydrolysis of oximes[11,12], a polar mechanism may be proposed for the oxidation of oximes of heterocyclic ketones by pyridinium chlorochromate (**Scheme-I**) ruling out radical mechanism involving the formation of iminoxy radicals[8].

The mechanism involves a slow formation of a positively charged pyridinium chlorochromate ester between the substrate and the protonated pyridinium chlorochromate by the removal of water molecule as reported in the chromic acid oxidation of alcohols[23], oxidation of aldehydes by pyridinium fluoro-

ϕ = 2-Cl phenyl, 2-CH$_3$ phenyl, 2-OCH$_3$ phenyl, 4-Cl phenyl, 4-CH$_3$ phenyl, 4-OCH$_3$ phenyl and unsubstituted phenyl
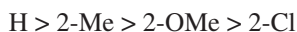
Scheme-I

chromate[24] acids by pyridinium chlorochromate[25], alicyclic ketoximes by PFC[12]. Hence in the light of these arguments a polar mechanism has been proposed.

Influence of structure on reaction rates: The reactivity trend observed for various oximes is:

For *para* substituted aryl compounds:

H > 4-Cl > 4-Me > 4-OMe

For *ortho* substituted aryl compounds:

H > 2-Me > 2-OMe > 2-Cl

This reactivity trend supports the proposed mechanism as the substituents at second and fourth positions of the aryl groups release electron density due to mesomeric effect and lower rates are expected in all the cases. A similar observation was made by Usha[26] and Shyamala[15] during the oxidation of similarly substituted acetophenone oxime.

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