

Oxidation of Oximes of Heterocyclic Ketones by Pyridinium Chlorochromate: A Kinetic and Mechanistic Study

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Kinetics of oxidation of 2,6-diphenyl piperidin-4-one and its 3-alkyl substituted derivatives by pyridinium chlorochromate has 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 rate decreases with decrease in 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 found to be PPO > 3-MePPO > 3-EtPPO > 3,3-diMePPO > 3-*ipr*PPO.

Key Words: Kinetic, Oxidation, Pyridinium chlorochromate, Oximes, Heterocyclic ketones.

INTRODUCTION

Oximes find application in industrial as well as medicinal areas. Regeneration of carbonyl compounds from its derivatives is an important process in synthetic organic chemistry. Oximes such as cyclohexanone oxime, benzophenone oxime and cyclohexadione oxime are employed as antifungal reagents for silicone rubber. Aliphatic ketoximes are used in the preparation of pesticides and antiglucoma agents while aromatic ketones find use as antimolding agents for leather. Oximes have been converted to the corresponding aldehydes or ketones by treatment with reagents like thallium(III)¹, manganese(IV)², 1-chlorobenzotriazole³, peroxomono-sulphate⁴, acid dichromate⁵, PFC⁶, NBSA⁷, NBS⁸ and QDC⁹. However extensive work in this field has not been carried out with the oxidant pyridinium chlorochromate (PCC). Hence in the present investigation the kinetics of oxidation of oximes of 2,6-diphenyl piperidin-4-one (PPO) and its 3-alkyl substituted derivatives *i.e.*, 2,6-diphenyl-3-methyl piperidin-4-one (3-MePPO), 2,6-diphenyl-3-ethyl piperidin-4-one (3-EtPPO) by pyridinium chlorochromate, 2,6-diphenyl-3,3-dimethyl piperidine (3,3-diMePPO) and 2,6-diphenyl-3-isopropyl piperidin-4-one (3-*ipr*PPO) have been chosen for study.

EXPERIMENTAL

Pyridinium chlorochromate (PCC) a complex of chromium trioxide and hydrochloric acid is prepared in the laboratory by the method cited in the literature¹⁰ and its purity was checked by iodometric method. A stock solution of PCC of strength 7.5×10^{-4} mol dm⁻³ was prepared in conductivity water. The oximes were prepared by the standard procedures^{11,12}. The oximes were recrystallized from suitable solvents. The purity of the sample was confirmed by comparing the respective physical constants with literature values which show good concordance. Acetic acid used for kinetic runs was thrice distilled by adopting the usual procedures¹³. All other chemicals used were of analytical grade.

Kinetic procedure: The measurements were carried out in 60 % (v/v) aqueous acetic acid medium under pseudo first order conditions. The reactions were carried out in the temperature range 278 to 308 K. The ionic strength of the medium was maintained at 0.021 mol dm⁻³ by using Na₂SO₄ and sulphuric acid. The progress of the reaction was followed spectrophotometrically at 355 nm up to 80 % completion of the reaction. The pseudo first order rate constants were evaluated and found to be reproducible within ± 3 %.

Test for free radical intermediates: No polymer formation was obtained when a freshly distilled acrylonitrile monomer 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 PCC was allowed to react with a known concentration of 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 oxidant: The dependence of rates of reaction on oxidant concentration was investigated by varying [PCC] in the range 2.5×10^{-4} - 12.5×10^{-4} . In all the reactions investigated the plots of log [PCC] vs. time (min) were found to be linear showing a first order dependence on [PCC]. However, the pseudo first order rate constants were found to decrease with increase in concentration of PCC (Table-1). Similar observations have been reported earlier in the oxidation studies involving other Cr⁶⁺ oxidants¹⁴⁻¹⁶.

Order with respect to oxime: The dependence of the rates of reaction on substrate concentration was studied by varying [oxime] in the range 0.5×10^{-3} - 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 ($\text{dm}^3 \text{mol}^{-1} \text{s}^{-1}$) were evaluated.

TABLE-1
RATE DATA FOR THE OXIDATION OF 3-Et-2,6-diphenyl piperidin-4-one oxime by PCC

[PCC] $\times 10^{-1}$ mol dm^{-3}	[3-Et PPO] \times $10^{-2} \text{mol dm}^{-3}$	[H ₂ SO ₄] \times $10^{-3} \text{mol dm}^{-3}$	μ mol dm^{-3}	AcOH: H ₂ O % (v/v)	$k_1 \times 10^{-4}$ (s^{-1}) Temp. 293 K
2.5	1.0	2.0	0.021	60:40	9.78
5.0	1.0	2.0	0.021	60:40	7.48
7.5	1.0	2.0	0.021	60:40	4.01*
10.0	1.0	2.0	0.021	60:40	3.16
12.5	1.0	2.0	0.021	60:40	1.46
7.5	0.75	2.0	0.021	60:40	3.29
7.5	1.25	2.0	0.021	60:40	5.37
7.5	1.5	2.0	0.021	60:40	6.37
7.5	3.00	2.0	0.021	60:40	12.53
7.5	1.0	0.5	0.021	60:40	3.28
7.5	1.0	3.0	0.021	60:40	4.23
7.5	1.0	4.0	0.021	60:40	4.78
7.5	1.0	2.0	0.018	60:40	4.51
7.5	1.0	2.0	0.024	60:40	3.49
7.5	1.0	2.0	0.027	60:40	3.38
7.5	1.0	2.0	0.021	40:60	13.47
7.5	1.0	2.0	0.021	50:50	4.75
7.5	1.0	2.0	0.021	70:30	3.18
7.5	1.0	2.0	0.021	80:20	2.68

*at 288 K, 2.49, at 298 K, 6.27, at 303 K, 9.38.

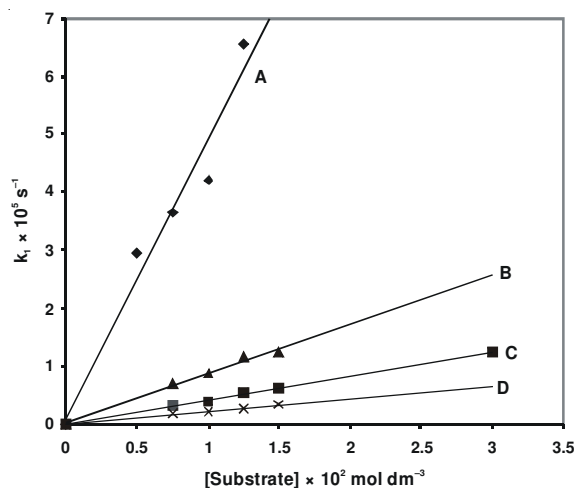


Fig. 1. Evaluation of k_2 at 293 K, A: 3-MePPO, B: 3-EtPPO, C: 3,3-diMe₂PPO, D: 3-iprPPO

Effect of $[H^+]$: The acidity of the medium was varied from 1×10^{-3} - 4×10^{-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 $\log k_{\text{obs}}$ 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 step¹⁷.

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 40-80 % (v/v). The reaction rates were found to decrease with decreasing dielectric constant of the medium. This is consistent with the fact that the charge density is delocalized in the transition state.

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), ΔG^\ddagger (kJ mol⁻¹) ΔH^\ddagger (kJ mol⁻¹) and ΔS^\ddagger (Jk⁻¹ mol⁻¹) have been computed and presented in Table-2.

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

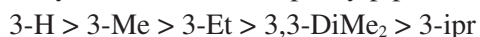
Substrate (- 278 K)	[Substrate] = 1×10^{-3} mol dm ⁻³ , $\mu = 0.021$ mol dm ⁻³ ,			[PCC] = 7.5×10^{-4} mol dm ⁻³ , AcOH = 60 % (v/v)	
	$-k_2$ 283 K ($\times 10^2$ 288 K)	dm ³ 293 K (mol ⁻¹ 298 K)	s ⁻¹ 303 K (- 308 K)	E _a kJ/mol (ΔH^\ddagger kJ/mol)	ΔS^\ddagger kJ/mol (ΔG^\ddagger kJ/mol)
3-EtPPO	-	4.15	10.07	64.26	-51.00
(-)	(2.04)	(5.68)	(-)	(61.83)	(79.56)
PPO	16.81	50.19	-	56.64	-65.52
(-)	(30.32)	(75.60)	(-)	(54.21)	(73.41)
3-MePPO	20.80	45.48	-	58.43	-46.50
(18.76)	(35.56)	(-)	(-)	(55.99)	(69.62)
3- <i>i</i> pr PPO	-	0.23	0.29	33.57	-189.93
(-)	(-)	(0.25)	(0.352)	(31.13)	(86.76)
3,3-diMe ₂ PPO	-	0.75	2.46	69.60	-54.79
(-)	(0.52)	(1.66)	(-)	(67.19)	(83.24)

Mechanism: In the light of all the experimental results obtained in the present investigation and the evidences from the other investigations involving the oxidative hydrolysis of oximes^{5,6}, a polar mechanism may be proposed for the oxidation of oximes of heterocyclic ketones by PCC ruling out radical mechanism involving the formation of iminoxy radicals¹.

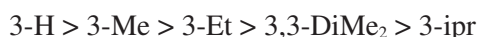
The mechanism involves a slow formation of a positively charged PCC ester between the substrate and the protonated PCC by the removal of water molecule as

reported in the chromic acid oxidation of alcohols¹⁸, oxidation of aldehydes by PFC¹⁹ acids by PCC²⁰ and alicyclic ketoximes by PFC⁶. Hence in the light of these arguments a polar mechanism has been proposed.

Influence of structure on reaction rates: The reactivity trend observed for oximes of different 3-alkyl substituted 2,6-diphenylpiperidin-4-one is



It is observed that the reactivity decreases as the size of the alkyl substituent increases. This indicates that there should be more steric crowding in the transition state than in the ground state. It is evident that the increase in the steric crowding is proportional to the bulkiness of the substituent in the third position. That is why the reactivity decreases in the order



The inductive effect of the substituents increase in the same order which may decelerate the reaction by reducing the positive charge of the central carbon atom. Thus the reactivity trend can be accounted by both steric²¹ crowding and inductive effect.

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