



## Oxidative Deoxygenation of N-Methyl-2,6-diphenyl piperidin-4-one Oxime and Its 3-Alkyl Derivatives by Acid Dichromate

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Kinetics of oxidation of N-methyl-2,6-diphenyl piperidin-4-one and its 3-alkyl substituted derivatives by acid dichromate has been studied in aqueous acetic acid medium. The oxidation is first order with respect to [oxidant] and [substrate]. The reactions are acid catalyzed. Ionic strength has no appreciable effect on the reaction rate. The reaction rate decreases with decrease in the dielectric strength of the medium indicating a polar mechanism. The reactions followed at four different temperatures and the activation parameters computed. Based on the results obtained a suitable mechanism is proposed. The reactivity sequence is found to be 1,3,5-trimethyl PPO > 1-methyl PPO > 1,3-dimethyl PPO > 1-methyl-3-ethyl PPO > 1-methyl-3-isopropyl PPO.

**Key Words:** Deoxygenation, N-Methyl-2,6-diphenyl piperidine-4-one, Oxime, Pyridinium chlorochromate, Kinetics.

### INTRODUCTION

Regeneration of carbonyl compounds from its derivatives under mild conditions is an important process in synthetic organic chemistry. Conversion of oximes to their respective carbonyl compounds by treatment with reagents like aqueous titanium(III) chloride<sup>1</sup>, aqueous sodium bisulphate<sup>2</sup>, iron pentacarbonyl and boron trifluoride<sup>3</sup>, selenium hydride<sup>4</sup>, phenyl iodoacetate<sup>5</sup>, N-chloro piperidone<sup>6</sup> and diperiodato argentate<sup>7</sup> have been reported. Kinetics of regeneration of carbonyl compounds from their oximes and semicarbazones with various reagents have been reported<sup>8-12</sup>. Oxidative hydrolysis of oximes of aromatic ketones, aliphatic ketones and alicyclic ketones have been studied with acid dichromate<sup>13</sup>. The literature survey revealed that no work on the oxidation of entitled oximes with acid dichromate is reported. Hence in the present investigation it is proposed to study the kinetics of oxidation of N-methyl-2,6-diphenyl piperidin-4-one oxime and its 3-alkyl substituted derivatives.

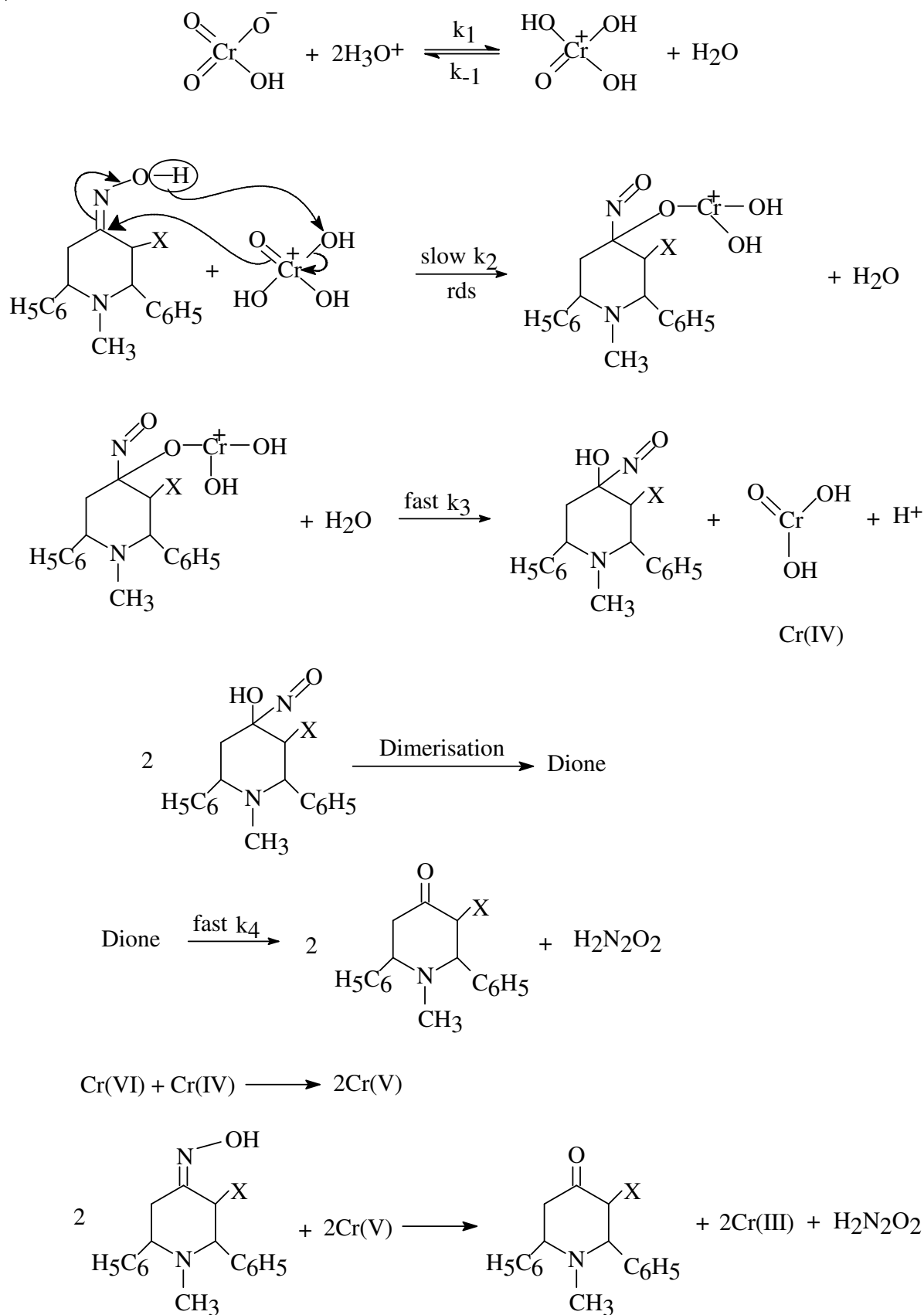
### EXPERIMENTAL

AnalaR Glaxo sample of potassium dichromate was dissolved in water to give a stock solution of strength  $1 \times 10^{-2}$  mol dm<sup>-3</sup> as it is a primary standard. All oximes are prepared by following the procedure given in the literature<sup>14,15</sup>. Acetic acid used as solvent in the kinetic studies was purified by the usual procedure<sup>16</sup>. All chemicals used were of analytical grade.

**Kinetic procedure:** All the rate measurements for oximes were carried out in 60 % (v/v) aqueous acetic acid medium. The kinetic runs were followed, under pseudo first order conditions. The acidity of the medium and ionic strength were maintained constant by using sulphuric acid ( $5 \times 10^{-3}$  mol dm<sup>-3</sup>) and sodium sulphate ( $5 \times 10^{-3}$  mol dm<sup>-3</sup>), respectively. The course of the oxidation was followed by monitoring the disappearance of Cr(VI) spectrophotometrically at 355 nm for 80 % completion of the reaction. The pseudo first order rate constants were evaluated from the slopes of the plots of log O.D versus time in minutes. The results were found to be reproducible within  $\pm 3$  %. The activation parameters were computed by carrying out the kinetic experiments at four different temperatures (288-303 K).

**Stoichiometry and product analysis:** The stoichiometry of the reaction was determined by allowing a known excess of acid dichromate to react with the substrate in presence of aqueous acetic acid -H<sub>2</sub>SO<sub>4</sub> at room temperature. The unreacted dichromate was estimated spectrophotometrically after 24 h. The stoichiometry was found to be in the mole ratio of 1: 1 for oxidant to substrate. 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 and IR spectroscopy.

**Test for free radical intermediates:** When a freshly distilled acrylonitrile monomer was added to deaerated reaction mixture no polymer formation was observed indicating the absence of free radical intermediates.



X = -H, -Me, -Et, -*iso*-Pr, -3,5-diMe

Evaluation of  $k_2$  at 293 K, A-3-*iso*Pr PPO; B-3-EtPPO; C-3-MePPO; D-3-H PPO; E-3,5-diMePPO

Scheme-I

## RESULTS AND DISCUSSION

**Order with respect to oxidant:** The influence of the oxidant on the rate of the reaction was studied by varying  $[K_2Cr_2O_7]$  in the range  $1.00 \times 10^{-4}$ - $7.00 \times 10^{-4}$  mol dm<sup>-3</sup>. In all the reactions investigated, the plots  $\log [Cr(VI)]$  versus time were found to be linear showing a first order dependence on  $[Cr(VI)]$ . However, pseudo first order rate constants were found to decrease with increase in concentration of  $K_2Cr_2O_7$  (Table-1). Similar observations have been reported earlier in the oxidation studies involving other  $Cr^{6+}$  oxidants<sup>17-19</sup>.

**Order with respect to substrate oxime:** The dependence of the rates of reaction on substrate concentration was studied by varying [oxime] in the range of  $0.75$ - $1.50 \times 10^{-2}$  mol dm<sup>-3</sup> and fixed concentrations of the other reactants. The plots of  $\log K_2Cr_2O_7$  versus time (min) at different initial concentration of oxime but at fixed concentration of  $K_2Cr_2O_7$  were linear and the value of  $k_{obs}$  (s<sup>-1</sup>) evaluated from slopes were found to be dependent on the initial concentrations of the substrate. The plot of  $\log k_{obs}$  versus  $\log [oxime]$  was linear with unit slope showing a first order dependence on [oxime]. The values of  $k_{obs}$  (s<sup>-1</sup>) 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<sup>3</sup> mol<sup>-1</sup> s<sup>-1</sup>) were evaluated.

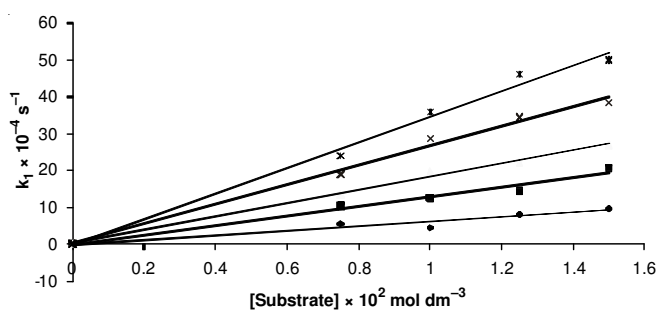


Fig. 1

**Order with respect to  $[H^+]$ :** To investigate the effect of acidity on reaction rate the kinetic runs were performed at

different  $[H^+]$  ion concentrations ranging from  $4.00 \times 10^{-3}$ - $7.00 \times 10^{-3}$  mol dm<sup>-3</sup> keeping the ionic strength constant. The oxidation reactions were found to be acid catalyzed. The plots of  $\log k_1$  against  $\log [H^+]$  are linear and the values of the slopes indicated a fractional order.

**Effect of ionic strength:** The influence of ionic strength by added neutral salt was studied by varying the ionic strength from 0.027-0.036. The negligible effect of ionic strength on reaction rates indicated the interaction of an ion and a dipole in the rate determining step<sup>20</sup>.

**Dependence on solvent polarity:** The dependence of reaction rate on solvent polarity was evaluated by varying the percentage of acetic acid in the range 40-70 % (v/v). The reaction rates were found to decrease with decreasing dielectric strength of the medium. This trend reveals that the charge density is delocalized in the transition state.

**Effect of temperature and activation parameters:** From the kinetic results it was clear that the second order rate constants increase with increase in temperature. The plots of  $\log k_2$  versus  $1/T$  were linear indicating that the Arrhenius law is being obeyed. The thermodynamic parameters were computed and presented in Table-2.

**Mechanism:** The oxidation reactions are catalyzed by acid. The enhancement of oxidation rate with acidity suggests the involvement of a protonated species<sup>18</sup>. The participation of such species is well known in oxidation reactions of  $Cr(VI)$  oxidant<sup>9,13</sup>. The mechanism involves a slow formation of a positively charged ester between the oxime and protonated oxidant by the removal of water molecule as reported in the chromic acid oxidation of alcohols<sup>21</sup>, oxidation of aldehydes by pyridinium fluorochromate<sup>22</sup>, acids by pyridinium chlorochromate<sup>23</sup>, alicyclic ketoximes by pyridinium fluorochromate<sup>9</sup>. Hence in the light of these arguments a polar mechanism has been proposed.

**Influence of structure on reaction rates:** From the magnitude of the rate constants, the reactivity trend observed for oximes of 1-methyl-2,6-diphenyl piperidin-4-one and some of its 3-alkyl substituted derivatives is

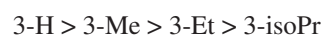


TABLE-1  
RATE DATA FOR THE OXIDATION OF N-Me-3-Et-2,6-DIPHENYL PIPERIDIN-4-ONE OXIME BY ACID DICHROMATE

$Cr(VI) \times 10^{-4}$ (mol dm <sup>-3</sup> )	N-Me-3-Et PPO $\times 10^{-2}$ (mol dm <sup>-3</sup> )	$[H_2SO_4] \times 10^3$ (mol dm <sup>-3</sup> )	$\mu$ (mol dm <sup>-3</sup> )	AcOH: H <sub>2</sub> O	$k_1 \times 10^{-4}$ (s <sup>-1</sup> )
1.0	1.0	5.0	0.030	60:40	18.40
3.0	1.0	5.0	0.030	60:40	11.50*
5.0	1.0	5.0	0.030	60:40	9.90
7.0	1.0	5.0	0.030	60:40	6.10
3.0	0.75	5.0	0.030	60:40	8.40
3.0	1.25	5.0	0.030	60:40	14.40
3.0	1.5	5.0	0.030	60:40	20.70
3.0	1.0	4.0	0.030	60:40	7.70
3.0	1.0	6.0	0.030	60:40	15.40
3.0	1.0	7.0	0.030	60:40	23.00
3.0	1.0	5.0	0.033	60:40	11.00
3.0	1.0	5.0	0.036	60:40	10.80
3.0	1.0	5.0	0.027	60:40	12.20
3.0	1.0	5.0	0.030	40:60	26.30
3.0	1.0	5.0	0.030	50:50	16.50
3.0	1.0	5.0	0.030	70:30	6.30

\*at 288 K, 8.4; at 298 K 17.90; at 303 K 28.80.

TABLE-2  
RATE CONSTANTS AND ACTIVATION PARAMETERS FOR THE OXIDATION OF OXIMES  
[Substrate] =  $1 \times 10^{-2}$  mol dm<sup>-3</sup>, [Cr(VI)] =  $3.0 \times 10^{-4}$  mol dm<sup>-3</sup>,  $\mu$  = 0.030 mol dm<sup>-3</sup>, AcOH = 60 % (v/v)

Substrate	$K_2 \times 10^{-2}$ (dm <sup>3</sup> mol <sup>-1</sup> s <sup>-1</sup> )				Ea (kJ/mol)	$\Delta H^\ddagger$ (kJ/mol)	$\Delta S^\ddagger$ (J/K/mol)	$\Delta G^\ddagger$ (kJ/mol)
	288 K	293 K	298 K	303 K				
1-Me-3-Et PPO	8.40	11.50	17.90	28.80	57.44	55.01	-235.47	69.77
1-Me PPO	22.10	28.80	32.20	36.00	42.54	40.11	-238.03	69.04
1,3-diMe PPO	14.40	19.70	23.00	38.40	54.70	52.27	-235.38	69.28
1-Me-3-isoPr PPO	2.90	4.40	7.70	11.50	76.58	74.05	-233.02	70.05
1,3,5-triMe PPO	28.40	36.00	50.40	65.80	38.29	35.86	-238.98	68.34

The reactivity trend decreases as the size of the alkyl substituent increases indicating more steric crowding in the transition state. The inductive effect of the substituent also increases in the same order. Thus the reactivity trend can be accounted by both steric<sup>24</sup> crowding and inductive effect.

The rate constant for 1,3,5-trimethyl-2,6-diphenylpiperidin-4-one oxime with two adjacent methyl groups to the reaction centre is expected to be considerably lower than 1-methyl-2,6-diphenylpiperidin-4-one oxime but quite unexpectedly the rate is higher. This may be due the difference in conformation of this oxime<sup>15</sup>. This particular oxime has been shown to adopt a non-chair conformation by spectral studies.

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